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THE PROBLEM OF CALCIFICATION.[1]

By F. S. HANSMAN, M.B., Ch.M. (Sydney), M.R.C.P. (London),
Sydney.

To crystallize in a brief review our knowledge of the process of calcification is comparable with compressing carbon into a diamond. My crystal will be full of flaws and its facets unpolished. I beg your indulgence for the former and shall leave subsequent speakers to polish the latter.

No attempt will be made to give an historical survey of the subject (the reader may consult Keith,[44] Ham,[28] Harris[30]), nor will more than brief mention be made of pathological calcification (for a recent comprehensive review see Barr[3]) or of clinical diseases of the skeleton. Many theories concerning various unsettled points will be almost neglected, not that they are unimportant, but because a critical survey would divert us from what appears to be the more direct solution of the problem.

[1] Read at the annual meeting of the British Medical Association, Melbourne, September, 1935.

HISTOGENESIS OF BONE.

In order that we may visualize the same things and talk the same language, I would ask your forbearance during a short description of osteogenesis, taken from the works of Fell,[25] Stump,[104] Maximow and Bloom,[49] Brash,[13] Theiler,[108] Dodds[22] and Cajal.[17] In this brief account the intimate histological details of the cellular components will not be elaborated.

Histogenesis of Bone Laid Down in Cartilage.

The first differentiation of tissue that is to be the future bone of a limb is a condensation of mesenchymal cells, which have been shown by Fell to be definitely cellular and not syncytial, as previously

held. The central cells of this prechondral mass soon become elongated in a direction at right angles to the mass of cells and become separated from each other by an intracellular substance — the first appearance of the cartilage matrix. According to Fell this intracellular substance is a secretion of the cartilage cells, but according to Retterer it is transformed cartilage cytoplasm. By further differentiation this primitive cartilaginous area assumes an elliptical formation with the convexities pointing to the future epiphyses (Figure I). This ellipse from now on represents the diaphysis and the convexities will become the diaphyseal plates. Meanwhile two other developments are proceeding: first, the primitive epiphyses are taking form by further proliferation of the original prechondral mass and by additional condensation of mesenchymal cells (the latter additions continuing till the joint clefts appear) (Stump[104]), and secondly, the first rudiments of a perichondrium appear as a lining of cells differentiated from the mesenchyme adjacent to the lateral periphery of the diaphyseal cartilage. The cells in the centre of the diaphysis undergo successive changes of mitosis, hypertrophy and shrinking [there is no proof that they are degenerated (Dodds[22])], and the remains of their cell bodies come to lie in the increasingly dense cartilage matrix, which can thus be considered to consist of a close intercellular spongework, the interstices of which are filled with shrunken cartilage cells. This same succession of changes proceeds in a distal and proximal direction, and thereby the primitive shaft takes form as a cartilaginous rod limited by a diaphyseal plate of active proliferating cartilage cells at either end in relation to the epiphyses. Meanwhile the mesenchymal cells lining the middle of the cartilaginous mass of the shaft differentiate further into the perichondrium — a tissue composed at this stage of an external layer of fibroblasts and an internal layer of cells which soon differentiate into blood-forming elements (vessels and cells) and osteoblasts. Proximally and distally in the vicinity of the epiphyses the perichondrium fades into undifferentiated mesenchyme. With the attainment of this degree of differentiation in its central portion the perichondrium is termed periosteum (Figure II). The perichondrium progressively differentiates into periosteum proximally and distally *pari passu* with the progressive transformation into cartilage of the growing diaphyses, while in the vicinity of the developing epiphyses the perichondrium passes into the components of the developing joints.

Ossification (Figures II and III) begins as a sheaf of lamellæ composed of fibrils in an amorphous matrix round the central mass of cartilage of the shaft. Bone salts soon appear in this early osteoid tissue. These lamellæ run longitudinally, and as the osteoblasts of the periosteum move outwards further layers of lamellæ are laid down and form a hollow cylinder of compact bone, and bone corpuscles — cells which were originally osteoblasts—become occluded amongst the lamellæ. The cellular components of the periosteum now become appreciably thicker, and vascular channels develop; these come to lie in further deposits of bone which form trabeculæ running more or less transversely. A second very imperfect cylinder of bone, concentric to but outside of the first cylinder, is laid down directly beneath the laterally displaced fibrous periosteum. By a progression of these changes the whole of the developing shaft becomes lined by a series of incomplete tubes composed of trabeculæ surrounding blood vessels. These tubes are continuous on the one hand with the original primitive shaft of bone and on the other with the imperfect sheath of lamellæ beneath the fibrous periosteum.

The cartilage enclosed by the primitive sheath of bone (Figure IV) is now invaded by blood vessels which in mammals carry an osteogenic mesenchyme, but in birds this latter component is absent and the original cartilaginous mass is replaced by marrow only. In mammals osteoblastic activity results in the formation of bony trabeculæ, cartilaginous models cut out by the process of erosion which precedes the extension of the developing blood vessels being used as scaffolding. Along with the development of the hæmoblastic cells osteoclasts appear; these multinucleated cells are generally found in relation to cartilage and bone that is to be resorbed. By the extension of the blood vessels of the marrow towards the ends of the bone the cartilaginous shaft is eroded into channels to the vicinity of the diaphysis. The chief agent in causing solution of the cartilage appears to be the endothelial cells of the invading blood vessels, though Dodds[22] believes that they remove only the cartilage cell capsule and that osteoclasts remove the cartilage (Figure V). The cartilaginous

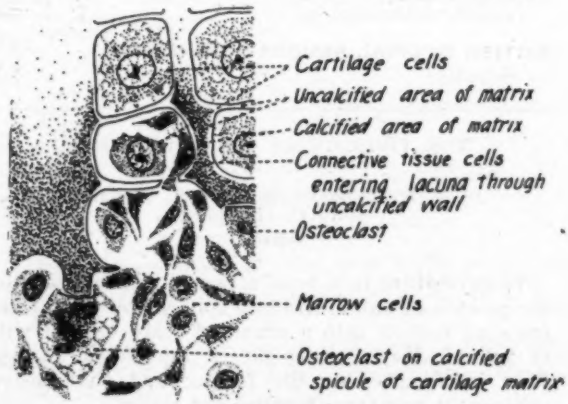
Cartilage cells
Uncalcified area of matrix
Calcified area of matrix
Connective tissue cells entering lacuna through uncalcified wall
Osteoclast
Marrow cells
Osteoclast on calcified spicule of cartilage matrix

FIGURE V.

Drawing to show essential features of destruction of cartilage in endochondral ossification. Calcified portion, with dark shading, being destroyed by osteoclasts; non-calcified portions, unshaded, by small cells of marrow, some of which are seen entering a lacuna beside the contained cartilage cell. From caudal vertebra of eighteen-day kitten. (From Dodds.)

scaffolds become lined by osteoblasts and a deposition of bone salts appears. By this stage the cartilage cells of the ends of the bone have taken

on their characteristic arrangement and consist of a diaphyseal zone of hypertrophic cells adjacent to the advancing blood vessels of the shaft, an intermediate layer of round cells, and a layer of flattened cells passing at first imperceptibly into the cells of the epiphysis, but later showing a somewhat marked delineation from the epiphyseal cells and a definite linear arrangement. The epiphysis at this stage consists of a somewhat narrow, flattened cup of cartilage cells, the ground substance of which is somewhat more basic than that of the diaphyseal cartilage (Fell[25]). The epiphysis is separately vascularized by the invasion of blood vessels from its external surface. As each successive layer of fully developed hypertrophic cartilage cells and of matrix materializes, the process of erosion by the endothelial blood vessels, the formation of cartilaginous scaffolding, the appearance of osteoblasts and the deposition of bone salts to form early bone trabeculæ, and the gradual development of cancellous bony trabeculæ go on serially and rapidly, so that the whole shaft becomes osseous, except in the region of the epiphyses and diaphyseal plates. Ultimately the whole of this cancellous bone and also the primitive periosteal bone are doomed to resorption (Figure VI). In the shaft of the mature

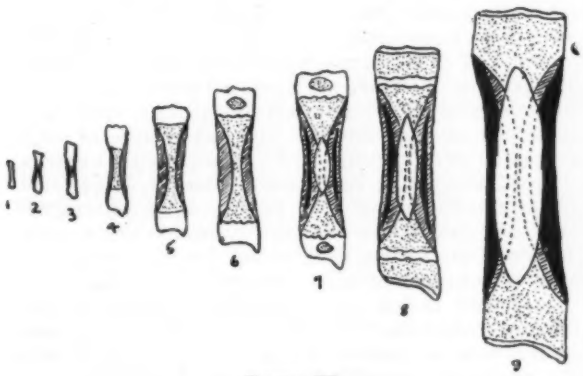

FIGURE VI.

Diagram of successive phases of development of a long bone (tibia). White = cartilage, stippled = endochondral bone, cross-hatched = periosteal bone, black = compact bone. 1: cartilage model; 2: the periosteal bone band in the centre of the diaphysis; 3: the primary point of endochondral ossification in centre of the cartilaginous diaphysis, meanwhile the periosteal bone has become thicker and longer; 4: the centre of the diaphysis is now entirely of endochondral bone in the shape of an hour-glass and is covered with an outer coat of periosteal bone; 5: the bone increases in size; 6: the point of secondary endochondral ossification appears in the cartilage of the upper epiphysis; 7: the same happens in the lower epiphysis, meanwhile compact bone (black) appears in the diaphysis and a bone marrow cavity in the centre (the former limits of the periosteal bone are indicated by the dotted line); 8: the epiphyses and diaphysis are separated by thin cartilaginous plates; 9: the epiphyses and diaphysis have fused; the latter is formed almost entirely of compact bone; the large bone marrow cavity has arisen at the expense of endochondral (stippled), periosteal (cross-hatched) and compact (black) bone. (From Maximow and Bloom.)

bone we have only laminated bone of Haversian systems, which have themselves replaced other earlier Haversian systems the vestigia of which are recognizable as intermediary lamellæ and cement lines interrupting the regularity of the mature Haversian systems.

Membrane Bone.

The histogenesis of membrane bones has recently been discussed by Brash,[13] who emphasizes that their development is closely analogous to the periosteal growth in long bones. Growth in all directions is due solely to the osteogenic activity of their periosteum, and there is no growth at the sutures. Brash[13] illustrates from his experimental work how in many cases the actual sutural line, as in the sutures of the zygomatic arch and in the mandible, actually change their place in order to maintain their relative positions. Brash stresses in this respect that resorption and deposition are of equal importance in the growth, not only of membrane bones, but of all bones. This point will be further discussed.

A Consideration of Certain Components of Bone.

Osteoblasts.—We must now consider certain components of bone in detail. First, the osteoblasts. Without describing the cytology, we may consider their distribution. They are probably present wherever bone is being laid down, though they may not necessarily arise from embryonic osteogenic mesenchyme. Thus Huggins[35] found them in bone that developed when urinary vesical epithelium was transplanted into the connective tissue of the abdominal wall (experimental animal, the dog). They have been described in aberrant sites of ossification, as in arteries, *myomata uteri*, tuberculous glands, in the kidney of the rabbit after ligation of the renal vessels *et cetera*. Maximow[48] remarks in this connexion that "in various pathologic conditions bone may be formed anywhere in the body by metaplasia of ordinary loose connective tissue". The stimulus that evokes their development is not apparent. Their function will be considered later.

The Osteoclast.—The origin of this multinucleated giant cell has been in dispute. Fell[25] agrees with Arey that in the fowl osteoclasts arise by fusion of cells indistinguishable from osteoblasts. Cajal,[17] Stump,[104] Maximow[49] and many others believe that they arise by the fusion of monocytes; others, for example, Lacoste, quoted by Fell[25] and Harris,[30] state that they arise from a single cell by nuclear division. There is almost a consensus of opinion that they are able to cause resorption of the whole structure of bone (for a recent detailed account of the process see Dodds[22]), though it is believed that bone can be resorbed without their aid, as in rapidly growing tumours of bone.

Diaphyses.—It must be clearly understood that the shaft of a bone grows at the diaphyses. This fact is clearly brought out by anatomists (Keith,[43] Stump,[104] Brash,[13] Maximow,[49] Fell[25] *et cetera*), but a certain looseness of expression has developed in other spheres, especially in relation to rickets. The epiphysis has a different morphological history from the diaphysis, and this distinction should be more rigidly observed.

The Periosteum at the Growing Ends of Bone.—The periosteum at the growing ends of bone deserves special attention. In this locality, as stressed by Keith,[43] the osteogenic periosteum

forms a ring around the core of diaphyseal cartilage and is responsible for the growth in length of the cortex of the shaft. When there is arrest of growth of this ring, areas of diaphyseal cartilage-formed bone become exposed on the surface of the shaft, and in the absence of the remodelling function of the periosteal cells is able to expand in abnormal directions, and there results the disease multiple exostoses (diaphyseal aclasis, Keith[43]), just as failure of the diaphyseal mechanism is the cause of achondroplasia.

The Matrix of Bone.—The matrix of bone (Figures VII and VIII) receives on the whole scant attention in books of histology, and it certainly has not received the attention from the chemist that is its due. Histologically bone matrix, that is, osteoid, in stained decalcified bone has a characteristic appearance, and its presence is taken as proof of the presence of bone. In other words, bone salts are deposited only in relation to this peculiar ground substance.

FIGURE VIII.
Diagram of the direction of the fibrils in successive plates of an Haversian system. Redrawn and slightly modified from Gebhardt. (From Maximow and Bloom.)

Microscopically this substance, as found in the lamellæ of the Haversian systems, is described as consisting of two zones, one granular and dark, the other showing brilliant longitudinal striations. This appearance is due to the fact that the lamellæ consist of fibrillar bundles which run in two directions, one forming longitudinal spirals, the other horizontal spirals, and the section cuts across bundles running in different directions to the plane of the section. These bundles of fibrils are embedded in an amorphous binding substance (Maximow,[49] Cajal[17]). The chemical composition of the individual components of this organic matrix is apparently not known. Taken as a whole, osteoid forms some 33% of the total weight of dried fat-free bone (*"Tabellæ Biologicæ"*,[105] Bogert and Hastings[12]) and consists of collagen indistinguishable from ordinary connective tissue collagen. This bone collagen or ossein gives gelatin on boiling, and so is highly proteinous. Small amounts of osseomucoid and osseo-albuminoid are also present (Hawk and Bergeim,[81] Maximow[49]). The actual site where the bone salts are deposited in the osteoid is unknown. Ebner (quoted by Cajal[17]) and Maximow state that they are deposited in the amorphous ground substance. Cajal[17] teaches that it is compounded with the fibrils. Whether the bone salts form a loose chemical combination with or are adsorbed by certain constituents of osteoid is unknown. Robison and Rosenheim[80] stress the importance of ascertaining the actual pH of osteoid *in vivo*. It is known to be basic to stains (Fell[25]). However, the problem of determining the actual reaction at the time of salt deposition is extremely difficult (Robison[87]). Further consideration of certain characteristics of osteoid tissue will appear in a later section.

BONE SALTS.

We next pass to a consideration of the chemical composition of the bone salts. The elucidation of the nature of the inorganic components of bone is not yet an accomplished fact. There has been a great deal of work done, every known mode of approach having been used, but though it is generally agreed that the elementary analysis of bone salts from practically any source denotes the presence of calcium, magnesium, sodium, potassium, phosphorus, fluorine, chlorine, carbon dioxide and water, there is no agreement as to how these are combined or as to whether only one or several salts are separately precipitated. The inorganic salts form two-thirds of the mass of dried fat-free bone (*"Tabellæ Biologicæ"*,[105] Bogert and Hastings,[12] Robison[87]) and the principal components are combinations of calcium with phosphate and carbonate and of magnesium with phosphate. Robison,[87] in a recent review of the problem, considers that improved quantitative analyses of all the elements in the same specimen of bone are required before the molecular constitution of the bone salts can be attempted; Washburn and Shear[111] have recently worked out accurate analytical methods for calcium, phosphorus and magnesium in the one specimen. Many workers[46][111][12] are removing the bone salts either without destroying the organic matrix or in such a way that there is no loss of elements by volatilization.

To deal with the problem in a systematic way, we begin with a paper by Bassett[4] in 1917, in which a review of earlier work is given. Bassett, from a long series of experiments on synthetic salts of calcium and on bone salts, concluded that, taking into consideration (i) the presence in serum of magnesium, potassium, sodium, carbonates and chlorides, and (ii) the reaction of the bone salt, the "mineral constituents of bone consist in the main of hydroxyapatite $(Ca_3P_2O_8)_3Ca(OH)_2$, mixed with a certain amount of $CaCO_3$. In addition to these chief constituents there are also small amounts of bicarbonates of Mg, Na and K which appear to be mainly adsorbed by the phosphate-

carbonate aggregate. The small amount of chloride also present is probably also adsorbed in the form of NaCl, although it may be present as chlorapatite."

Morgulis[55] studied the comparative elementary analysis of bones of marine fishes and a variety of higher vertebrates and found that the calcium carbonate of fishes is only about half that of the higher vertebrates, owing to the low carbon dioxide tension of fishes' serum and environment. He found that the calcium and alkalinity of bone were greater than would be required to satisfy formulæ such as provided by the ordinary salts of the apatite series, and concluded that $Ca(OH)_2$ is present in the bone salt, and proposed the formula $Ca[\{Ca_3(PO_4)_2\}_6](OH)_2$, a formula very similar to Bassett's.

The conception of a salt of the apatite series, that is, of a complex salt of calcium carbonate and calcium phosphate, is the most favoured. Sendroy and Hastings,[91] however, consider that $CaCO_3$ and $Ca_3(PO_4)_2$ exist separately and uncombined in any way.

Taylor and Sheard[106] criticize the conception of Sendroy and Hastings[91] and others who believe that $Ca_2(PO_4)_2$ is separately precipitated. They point out that pure $Ca_3(PO_4)_2$ has never been prepared in the laboratory—the laboratory product is usually too rich in calcium—and that it is unknown in nature.

These workers examined bone salts by the refraction index and by X ray diffraction photography. They quote De Jong as stating that the crystals in fresh untreated bone are so small that the X ray fringes are diffuse. They concluded from their own studies that the solid inorganic phase consisted essentially of very small crystals of apatite minerals of the general formula $3Ca_3(PO_4)_2CaX_2$, where X_2 ordinarily represents CO_3, Fe, $(OH)_2$, SO_4 and Ca, which may be to some extent replaced by Mg. Normal bone, dental enamel, dentine, rhachitic bone, bone low in phosphorus, salivary calculus and calcification of tuberculous lung were all found to have a similar structure.

Bogert and Hastings[12] analysed the cortex of bone by chemical methods which altered the original components as little as possible, and concluded that mature bone probably consists of a crystalline salt, $CaCO_3n(Ca_3(PO_4)_2)$, where n approximates 2 in untreated bone, that is, it is a salt of the nature of dahlite, a member of the apatite series.

Rosebury, Hastings and Morse,[88] by X ray analysis of bone and teeth, arrived at a similar formula, but gave the value of n as not less than 2 or more than 3.

From the purely chemical side there seems, therefore, a fair amount of agreement that the bone salt is a single substance of the nature of an apatite compound. Robison,[87] reviewing the situation up to 1931, agreed with an apatite salt, but considered that Mg, Na, K, Cl, Fe and OH were part of the complex carbonato-phosphate molecule.

From a survey of the work of a more biological nature the question of a single salt becomes more debatable. First, we have the evidence of Kramer and Shear,[46] who, using unashed bones of rats, have shown that the bone salt is not of constant composition and that primary calcification, which they found has the same composition in normal and in rhachitic animals, is lower in carbonates than older bones. Thus in young animals $CaCO_3$ forms 8% to 10%; in older animals, 15%. The residual Ca : P ratio remains constant at 1·99 in young and old animals.[1] They consider that the basic calcium in the freshly precipitated bone salt is due to the alkaline reaction at the site of deposition. This would be in keeping with certain conceptions of Robison[87] that there is an increased pH at the site of ossification, and the change in the type of bone salt with age may possibly be brought into line with the observation of Cameron[18] that the calcium of old bone does not stain with alizarin.

Howland, Marriott and Kramer[34] in 1926 showed that there was a higher $CaCO_3$ content in rhachitic than in normal bones, and Robison[87] gives an account of similar findings of Robison and Soames and of Korenchevsky and Roscoe. Brooke, Smith and Smith[15] found that rats fed on a diet poor in inorganic constituents lost calcium, phosphorus and carbonate from the bones, but that the loss of $CaCO_3$ was greater than that of $Ca_3(PO_4)_2$. Neal, Palmer, Eckles and Gullickson[57] fed cattle on various salt-deficient diets and found that $CaCO_3$ might be mobilized more readily than $Ca_3(PO_4)_2$ and that phosphorus might be stored in bones out of proportion to that amount of calcium that would be required if bone salt had a fixed composition as an apatite salt. The results of all these investigators indicate that salts of calcium, carbonate and calcium phosphate are precipitated independently.

The Blood in Relation to Calcification.

As the constituents of bone must be carried primarily by the blood stream, a very short account of certain metabolites must be given. The level of serum calcium in the human being is normally 9 to 11 milligrammes *per centum*. The amount does not seem to be affected appreciably by age or sex. The inorganic phosphorus is more variable, from 2·5 to 6·0 milligrammes *per centum* in the human being, and there is a definite diminution with advancing years. Different vertebrates show considerable variations in the amounts of calcium and phosphorus. The form in which calcium exists has been subject to much investigation. The most recent contribution to our knowledge is some work of McLean and Hastings,[58] who critically review the literature and conclude from their own experiments that the calcium in the serum is most simply thought of as existing as calcium proteinate, which ionizes as a weak electrolyte into calcium ions and protein ions, with a residue of un-ionized molecules, and that such factors as pH, albumin-globulin ratio,

[1] The residual Ca : P ratio is the amount of salt that would be present assuming that all the calcium not required by the CO_2 to form $CaCO_3$ would be present as $Ca_3(PO_4)_2$.

temperature, magnesium and citrate, and therefore presumably parathormone, play but a small individual and combined part. There has recently appeared a monograph by Fischer and Hooker,[25] in which a great deal of additional evidence is produced to show that serum is not a watery solution, but a lyophilic colloid, a solution of inverse type (Figure IX), in which, instead of the various substances present, for example, protein, lipoids and other organic and inorganic constituents, being dissolved in water, the water is dissolved in the protein, and the electrolytes exist to a large extent as combinations with the protein. Now the laws

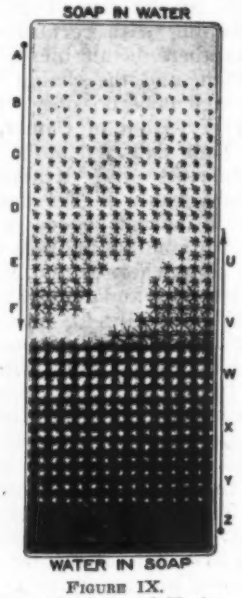

FIGURE IX.
From Fischer and Hooker.

governing the behaviour of simple solutions do not hold for solutions of inverse type, and until the laws that do hold are ascertained, it is useless to continue to try to fit the laws of simple solutions to the difficult problem of how various relatively insoluble substances exist in high concentration in serum. These workers have made out such a good case that I think with them that most of the previous work goes for nought and that a further discussion as to the importance to calcification of the supersaturation of serum with calcium phosphate and of the Ca × P product of the serum is a waste of time. Indeed, in the light of recent experimental work (for example, that of Shelling, Asher and Jackson[92]), the contention of Howland and Kramer[47] that calcification proceeds when the product Ca × P of the serum is greater than 30 can no longer be accepted. When we consider the infrequency of spontaneous calcification in the tissues, if it is ever spontaneous, and the absence of any precipitation of calcium phosphate in drawn serum allowed to stand indefinitely, we are led to conclude that, far from being in a state of supersaturation (Holt, La Mer and Chown[33]), the calcium and inorganic phosphate exist in serum in such stable forms that calcium phosphate can be precipitated only by the development of the highly specialized mechanism that will be discussed in the subsequent section. Furthermore, as is generally held—and to which balance experiments on a large variety of patients during the last four years at the Royal Prince Alfred Hospital lend strong support—the levels of serum calcium and phosphorus may tell nothing of the metabolism of calcium and phosphorus; there may be gross retention, gross loss or equilibrium of both these elements with perfectly normal serum concentration. In short, we have to explain the deposition of salts from a medium of whose chemistry relative to the problem in hand we know very little. But with what we have we pass to a study of the mechanism of calcification.

THE MECHANISM OF CALCIFICATION.

The researches of Robison and his collaborators at the Lister Institute, London, during the last ten years have given us a significant insight into the difficult problem of the mechanism of calcification. For an adequate survey of the work the original articles listed in references 67 to 86, Robison's book, "The Significance of Phosphoric Esters in the Metabolism",[87] and Kay's review, "Phosphatase in Growth and Disease of Bone",[42] may be consulted. In this paper we can unfortunately give only a brief summary of the mechanism as viewed by Robison at the present time. Let us consider the site at which ossification is proceeding, in the diaphysis of a limb bone. We have the two ground substances, cartilage matrix, a product of hypertrophic cartilage cells, and osteoid, a product of osteoblasts; both substances apparently have basic properties. The area is richly vascularized. The predominant cellular components are hypertrophic cartilage cells and osteoblasts. In the fluids bathing the region we have some 10 milligrammes *per centum* of calcium and some 3 to 5 milligrammes *per centum* of inorganic phosphate, and certain organic compounds of phosphorus. Now this same fluid bathes practically every other organ of the body, yet calcification occurs normally only in the bones. What local factors are responsible for precipitating the bone salts? Robison[87][80] has shown that there are at least two factors of essential importance, an enzyme and a second mechanism that favours the deposition of bone salts from supersaturated inorganic solutions. The enzyme concerned is a phosphatase, that is, it is able to hydrolyze certain compounds of alcohols and phosphoric acid. There are a very large number of phosphoric esters in Nature on which different phosphatases act more or less specifically. The bone phosphatase acts on a monophosphoric ester which is present in serum in a concentration of about 0·5 milligramme *per centum* in growing children. There is a relatively larger amount of suitable substrate in the erythrocytes, but whether this can be made available is not yet known. Robison[87] has shown that at the critical concentration of the inorganic radicals that exist at the site of calcification, the hydrolysis of the minute amount of organic salt

present in the serum is able to "increase the concentration of $PO_4^{\equiv}$ ions and the product of the concentration of $PO_4^{\equiv}$ ions and Ca^{++} ions then exceeds the solubility product of calcium phosphate, which becomes deposited in the organic ground substance of the tissue".

Now phosphatases are present in many other sites of the body (Kay,[42] Robison,[87] Martland, Hansman and Robison[78]) and it is reasonable to think that the concentration of $PO_4^{\equiv}$ ions must be increased in other places than in bone; again, in rickets, where there is an excess of bone phosphatase at the site of ossification, there is nevertheless a failure of the deposition of bone salts, so that the presence of phosphatase alone is not sufficient to cause calcification. The long series of experiments that led to the gradual recognition of a second mechanism that favours the precipitation of $Ca_3(PO_4)_2$ from its supersaturated solution cannot be detailed here. The actual nature of this mechanism is still not known. Robison suggests that it is bound up with some labile structure of the tissue colloids, but does not depend for its functioning on living cells, or that it may be an enzyme (Robison and Rosenheim[80]), but the fact that it was not totally destroyed by heating to 60° C. (Niven and Robison[85]) in certain experiments is rather against an enzyme. Some recent work by Miss Fischmann at the Strangeway Research Laboratory, Cambridge,[1] in which osteoid grown *in vitro* did not calcify normally in the serum of fowls fed on a diet deficient in vitamin *D* indicates that it is this second calcifying mechanism which is influenced by vitamin *D*. Robison has already shown that rhachitic bones are deficient in this second mechanism (Robison, McLeod and Rosenheim,[76] and Niven and Robison[85]), but he reserves his opinion as to whether the failure of the second mechanism to develop its full activity in rickets is due directly to lack of vitamin *D* or indirectly, from the results of this lack.[2] Vitamin *D* has no demonstrable effect on the calcification of bone slices *in vitro* (Robison and Rosenheim[80]).

Robison now thinks of the whole mechanism as an enzymic complex analogous to that in muscle or yeast (Robison and Rosenheim[80]). The development of this enzymic mechanism has an intimate relationship to the appearance of hypertrophic cartilage matrix and osteoid. The hypertrophic cartilage cells and the osteoblasts are responsible for the whole mechanism, so that, far from being senescent (Harris[30]), the hypertrophic cartilage cells are very active (Fell and Robison[86]). This calcifying enzymic complex is not present in cartilage that does not ossify (Fell and Robison,[79] Robison and Soames[75]) and is not present before the appearance of osteoid or hypertrophic cartilage cell matrix (Fell and Robison[86]).

The effect on the calcifying mechanism of bicarbonate (favourable), sodium chloride (inhibitory), potassium (indifferent), protein (inhibitory), glucose (inhibitory) has also been investigated by *in vitro* experiments.[87]

Magnesium plays a peculiar rôle. It greatly accelerates phosphatase activity (MacFarlane, Patterson and Robison,[84] Kay[42]), but inhibits the deposition of the bone salt (Robison,[87] Rosenheim[82]).

The optimum pH for the enzyme is quite high, about 9, though it is rapidly destroyed above 8·4. The question whether such a pH is obtainable at the site of calcification or whether such a pH is necessary for adequate functioning of the enzyme is fully considered (Robison[87]).

Recently Robison and co-workers have indicated something of the manner in which the pathological histology of rickets arises (Niven and Robison,[85] Rosenheim[83]). The calcifying power of the second mechanism is greatest when the cells have just attained full hypertrophy and then decreases when this stage has passed, so that if vitamin *D* is given to a rhachitic animal the regions of recently hypertrophied cells calcify densely, giving the appearance so well recognized in the "line test", while on the diaphyseal side of the shaft there remains a zone of disorganized tissue which is less readily calcifiable because the optimal stage of the calcifying mechanism has passed (Figure X).

In membrane bones (Fell and Robison[79]) and in heterotopic bones (Huggins[35]) this calcifying mechanism has also been demonstrated, and its appearance shortly precedes the actual deposition of the bone salts. The mechanism has also been demonstrated in teeth.[68] Calcification *in vitro* of non-osseous tissue, such as lung, kidney, bladder and aorta, where the presence of phosphatase has been demonstrated (MacFarlane, Patterson and Robison,[84] Rosenheim and Robison[81]) has been successfully attempted, and the results have been considered in relation to the problem of pathological calcification in these tissues.

Bone phosphatase has also been demonstrated in the plasma, probably gaining access by diffusion from the fluids in the vicinity where ossification is proceeding (Robison,[87] Kay[42]). Quantitative methods for diagnostic purposes have been elaborated (Kay,[42] Jenner and Kay,[38] Bodansky,[11] Morrell Roberts[66]) and a definite increase in the plasma has been demonstrated in certain bone diseases, for example, Paget's disease, von Recklinghausen's disease, osteomalacia.[10] The phosphatase is decreased in hypervitaminosis *D*,[42] but is normal in achondroplasia (Bodansky and Jaffe[10]). Recently Jean Smith[101][102] has demonstrated that plasma phosphatase increases in the plasma before rickets is demonstrable clinically, and she suggests that its quantitative estimation would be a valuable diagnostic aid before radiographic evidence is present. She further found that vitamin *D* administration to pre-rhachitic children who showed a raised plasma phosphatase value caused the value to keep to normal. On the other hand, children showing arrested growth, as in scurvy, had abnormally low phosphatase values.

[1] Commented on by Robison.
[2] Commented on by Robison.

Vitamin D.

We may now discuss the importance of vitamin *D* in more detail. Bills[8] in a recent review of the sterols points out that there are at least three distinct chemical substances that are antirhachitic; two are obtained by irradiating ergosterol, and the third is the naturally occurring substance in cod and other fish livers. These substances have quite different potencies for different animals.[103][7] The naturally occurring substance is more potent for fowls and humans than for rats. The actual function of vitamin *D* is still unknown. I reviewed the current theories up to 1932 (Hansman[29]) and shall deal here only with subsequent work. Kay and Guyatt[41] recently discussed the possibility of experimental rickets being a phosphorus deficiency disease. These workers[27] had previously described rickets produced by giving beryllium either with or instead of calcium, and were led to conclude that beryllium, by forming insoluble beryllium phosphate in the alimentary tract, caused a shortage of available phosphorus, which led to the rickets. Against this theory is some recent work by Sobel, Goldfarb and Kramer,[100] who indicate that in beryllium-fed or strontium-fed animals on diets deficient in vitamin *D* changes take place at the site of calcification which subsequently hinder calcification *in vitro*, as if these salts disturbed some local factor. Such an effect is not produced by vitamin *D* deficiency alone.

Taken with the experimental work elaborated in the section on "the mechanism of calcification", it seems that vitamin *D* influences the metabolism of calcium and phosphorus only indirectly, and probably only at the actual site where these elements are of value for tissue metabolism.

Further evidence against vitamin *D* acting by stimulation of the parathyreoid glands (Taylor *et alii*[107]) has accumulated from the results of Shelling *et alii*[92] and of Pugsley and Selye,[63] which indicate that, as far as calcification is concerned, vitamin *D* and parathormone have an antagonistic function.

It appears that though there is overwhelming evidence that vitamin *D* allows of normal calcification on otherwise rhachitogenic diets, and that it permits of the greatest economy in the metabolism of calcium and phosphorus, it is not absolutely essential for calcification if there are adequate quantities and proper proportion of calcium and phosphorus in the diet (Marek and Wellmann, quoted by Theiler[108]). Theiler considers that the importance of vitamin *D* is a species variant; it is important in some (for example, man, dog), unimportant in others (for example, bovines, equines, ovines[108]).

We may speculate whether vitamin *D* is an accelerator in some enzymic or analogous system, but must await further work to indicate its true position in the scheme of calcification. The laboratory history of vitamin *D* is, after all, the history of synthetic diets for experimental animals, and we shall revert to it again in a consideration of the effects of the level of inorganic salts in the diet.

The Interdependence of the Levels of Calcium, Phosphorus and Vitamin D in the Diet for Calcification.

Experiments to determine the effect on growth in animals receiving synthetic diets *plus* adequate vitamins, but in which the levels of calcium and phosphorus and the ratio of these two elements to each other were varied, have been carried out by a number of observers, the chief animal used being the rat. Only recent work will be discussed, as adequate reviews of previous work are available in articles subsequently quoted. Sherman and Quinn[94] found that with diets containing vitamin *D* and otherwise adequate, if either the calcium or phosphorus in the diet of rats were suboptimal, calcification, though normal, was retarded; that is, either of these elements would become limiting factors. Later, Sherman and Booher[95] studied the effects of synthetic diets in which the only variable was the amount of calcium in the diet (the diets contained from 0·16% to 0·50% calcium). It was found that the growth of the animal as a whole was unaffected, requiring a modification of Liebig's laws of the minimum, but that the bones, though of normal appearance, gave on analysis a lower ash content on the lower calcium intake. (This question will be further considered in dealing with the ideal diet for human beings.)

Shohl *et alii*[97] and Shohl,[98] using a diet (Steenboch and Black, Number 2,965) low in phosphorus but adequate in other respects, found normal calcification, but the animals were stunted and the bones were smaller and lighter than normal, so that low phosphorus had a more serious effect than low calcium.

In all these experiments as adult age was reached the bones acquired a normal percentage of ash.

In another article from the same laboratory (Brown, Shohl *et alii*[16]) the conclusion is reached that the ratio of Ca : P and the salt level are interdependent, and at a given fixed level of calcium or phosphorus increasing the amount of the other intensifies the degree of rickets in the absence of vitamin *D*, and in general the interference of calcification is evidenced by a fall in the amount of bone ash. Similar results were obtained by Bethke, Kick and Wilder,[6] who found that the optimal ratio of calcium to phosphorus was between 1 : 1 and 1 : 2.

The position in large domestic animals has been extensively investigated by Theiler and co-workers at Onderstepoort, South Africa.[108] One might epitomize their conclusions as follows. Skeletal disorders are found in bovines, ovines, equines, pigs, goats and dogs living under "natural" conditions in various parts of the world. These osteodystrophic diseases have analogies in human pathology, but though the histopathology is similar the exciting causes are apparently very different. He recognizes rickets and osteomalacia in bovines and ovines as the one disease, with age as the sole difference to account for the different histological findings. This same view is now accepted by students of human pathology, for example, Maxwell.[50] In bovines

and ovines rickets and osteomalacia are due solely to phosphorus deficiency and are the only nutritional skeletal diseases found in these species under "natural" conditions. The disease is known as aphosphorosis, pica disease, osteophagia, styfsiekte *et cetera*. Calcium deficiency, in distinction to phosphorus deficiency, in bovines and ovines leads only to stunted growth. In equines and goats a deficiency disease with a skeletal pathology indistinguishable from that of *osteitis fibrosa cystica* develops and is named by Theiler *osteodystrophia fibrosa*. (It is also called big head, osteoporosis, bran disease *et cetera*.) It is due to a relative excess of phosphorus to calcium in the diet, even though calcium is adequate. Theiler quotes the work of Kintner and Holt in the Philippine Islands as proving that the disease develops at a Ca : P ratio of 1 : 2·9, but not on a ratio of 1 : 1·9, and that the disease is independent of vitamins *A*, *B* or *D*.

Pigs may suffer from both diseases, that is, rickets or *osteodystrophia fibrosa*. Dogs may also suffer from both diseases, but the most frequent cause of skeletal disease is lack of vitamin *D*. This view is also held by Morgan *et alii* (A. F. Morgan[51][52][53][54]). The histopathology of the above diseases is very well described by Theiler. Neal *et alii*,[59] in an experimental study on cattle, also showed the untoward effect of low phosphorus in the diet.

Adult Animals.—Though the ratio of calcium to phosphorus in the diet is of greatest importance in growing animals, there is experimental evidence that disorders of the skeleton arise by salt deficiency in the adult. Theiler discusses this problem in large animals, while Klatzien, Templin and Steenbock[45] and Templin and Steenbock[109] have shown it experimentally in the rat.

In the human vitamin *D* seems to play the most important rôle in skeletal deficiency diseases (Eliot and Jackson[23]), but no attempt will be made to survey the literature on the pathology of human rickets. The problem of osteomalacia was recently reviewed by Maxwell.[50] In contrast to Theiler's findings in bovines, that fœtal rickets never occurs, no matter how advanced is the osteomalacia in the mother, Maxwell has definitely demonstrated that in the human the fœtus of an osteomalacic mother may show advanced rickets. Maxwell's cases of osteomalacia in China were apparently the result of a combination of factors—poor diet, low calcium and phosphorus and low vitamin *D*.

As far as the adult human, cattle and sheep are concerned, one may state that a drainage on bone salts is due to low mineral intake, which is accentuated by lack of vitamin *D*. In the horse an excess of phosphorus to calcium is the chief factor.

Hypervitaminosis D.

Lack of vitamin *D* causes one form of abnormal calcification, but excess causes another. Hypervitaminosis *D* has been most fully investigated in the dog. The chief features are a hypercalcæmia, an excessive excretion of calcium, and pathological calcification of tissues. The source of the calcium causing the hypercalcæmia has recently been reviewed by Jones *et alii*.[39] It is almost generally held that the bones are the chief source of this calcium, but Jones *et alii* concluded from their experiments, which consisted of giving vitamin *D* in excessive doses to dogs on a calcium-free diet and after a period of three weeks adding calcium, that the calcium came from the food. However, their protocols clearly indicate that even on a calcium-free diet there was a significant rise in serum calcium. No balance experiments were done, and the futility of drawing deductions from the level of calcium in the serum has already been stressed. Of more significance are the results of Reed *et alii*,[64] who, from an extensive series of experiments on dogs given excessive doses of vitamin *D*, found significant increases of calcium in aorta, brain, right and left ventricles of heart, muscles and spleen. Renal damage with subsequent calcification in that organ was the rule. Balance experiments for calcium and phosphorus were inconclusive.

Further work is therefore required to determine the actual pathology of hypervitaminosis *D* in relation to calcification.

The Effects on Calcification of the Secretions of the Endocrine Glands.

The injection of excessive quantities of certain hormones is known to produce definite metabolic changes, and while this does not necessarily mean that similar metabolic changes, but of less degree, are the normal response to the concentration of that hormone in circulating blood, investigations along such lines are important and their result as they concern our problem will be briefly considered.

Parathyreoid Glands.

There are many excellent reviews on the physiology of the parathyreoid glands and their importance to calcium and phosphorus metabolism (Aub,[1] Hunter,[36] Thomson and Collip,[110] Dragstedt[21]). Parathormone above normal requirements causes a mobilization of bone salts, by the resorption of bone trabeculæ, and we shall try to consider the *modus operandi*. Compere[20] has recently reviewed the accumulated clinical material and concluded that *osteitis fibrosa cystica generalisata* (von Recklinghausen) is the only disease that is associated with a pathological hyperactivity of the parathyreoid glands. He discusses the histology of the bones and points out that the appearances are not always pathognomonic, as they are frequently indistinguishable from *osteitis deformans* (Paget's disease), which is quite unassociated with any abnormality of parathyreoid function. He gives a useful table indicating the chief differential diagnostic features of a number of skeletal diseases. On the experimental side, Shelling *et alii*,[92] in rats (animals which are relatively very resistant to parathormone), concluded that in young rats on a stock diet injection of large doses of parathormone caused decalcification and fibrous tissue replacement, that

is *osteitis fibrosa*; on moderate doses calcification was definitely increased and hyperostosis resulted (Figure XI). On rhachitogenic diets the rickets was accentuated, but there was marked stimulation of attempts at osteogenesis. The rickets was further accentuated by decreasing the phosphorus in the diet; resorption of bone was present, but there was definite osteoblastic activity. Pugsley and Selye,[63] using adult rats as the experimental animal, found that parathormone caused resorption of bony trabeculæ associated with an osteoclastic reaction and that when a refractory stage to the effects of the hormone was reached, the osteoclasts disappeared and the mobilization of bone salts ceased (Figure XII). Several experimenters, notably Bodansky and Jaffe,[9] have produced typical *osteitis fibrosa cystica* by parathormone injections, but as Theiler[108] points out, cysts are not a pathognomonic feature but the result of mechanical forces. Morgan *et alii*[53] consider *osteitis fibrosa cystica* a manifestation of calcium lack. On the whole, the experimental evidence indicates that the physiological function of parathormone is to aid calcification at a stage subsequent to the primary calcification. It may possibly control to some extent the ultimate density of bone. In excessive doses it causes a mobilization of calcium salts from the trabeculæ by osteoclastic action.

Thyreoid Gland.

The effect of excess of circulating thyroxin in man has recently been discussed by Hansman and Wilson,[29] who concluded, contrary to the views of Aub and co-workers (Harvey Lectures[1]), that thyroxin *per se* had no effect on calcification. Barr, who discussed this problem recently with me, considers that there may be a second hormone in the thyreoid which is able to effect calcium metabolism. Pugsley and Anderson,[61] from experimental work on the rat, consider that thyroxin causes a mobilization of bone salts; but as their animals lost a good deal of weight, a phenomenon which is known to influence calcium and phosphorus balance, these results cannot be accepted as definite evidence of a decalcifying effect of thyroxin in the rat. The problem is still unsolved.

Thymus Gland.

Recently Rowntree *et alii*,[89] by injecting thymic extract (Hanson) into successive generations of rats, obtained an extraordinarily early maturity in the third and subsequent generations. In this precocity the animals matured as a whole, so that the skeleton was also affected. Further studies along these lines are eagerly awaited.

Pituitary Gland.

The profound stimulus to osteogenesis that results from excessive activity of the eosinophilic cells of the anterior pituitary is too well known to need further discussion. Very little recent work has been done on the way in which this effect is produced. Various aspects of the problem from a clinical aspect have recently been discussed by Ballin,[2] Englebach,[24] and Behrens and Barr.[5]

The Calcium and Phosphorus Requirements for Normal Calcification in the Human.

The problem of the calcium and phosphorus requirements for normal calcification in man may be approached from various angles. We can calculate the amount of calcium and phosphorus in the actual food consumed by a large number of children; this gives a rough indication of the amount that has been available for a process which is assumed to have gone on normally. We can calculate the total calcium content of the body, and assuming a fairly constant rate of retention, we can work out the requirements *per diem*. Lastly, we can do actual balance experiments, that is, we can feed humans at different ages on known diets and by analysing the total intake and excretion find out how much the organism retains. All these modes of approach have been used. This is not the place, however, to go into details, as calcium and phosphorus are required for other purposes than for calcification. Although 99% of the calcium is in the bones, it is probable that the other 1% is most active in a katabolic sense.

There are (by calculation from Table 186, Needham, "Chemical Embryology"[60]) some 28·9 grammes of calcium in the fœtus at term. Lusk,[48] using Michel's data, gives 30·51 grammes of calcium; Harding, quoted by Sherman,[93] gives 30 grammes. The average calcium content of the skeleton at the twentieth year, calculated from Ingalls's data[37] and using Morgulis's tables for the calcium content of macerated bone (*"Tabulæ Biologicæ"*[105]), is 723 grammes; using data from Bogert and Hastings[12] there are 792 grammes of calcium; so that by calculation the growing child adds on an average some 0·101 to 0·104 gramme of calcium *per diem* to the skeleton. It is true that growth is irregular, but nevertheless, taking all the factors of growth and increasing size into consideration, this is probably a fair value of the minimal requirements for bone growth from day to day.

If now we determine the minimal katabolic excretion of calcium, assuming maximal ability to absorb and retain calcium, we should have some approximation of the absolute minimal requirement of calcium for growth. In the course of our investigation at the Royal Prince Alfred Hospital we have come across children who at the time of the experiment were retaining calcium to a marked extent, or we might say the ability to utilize calcium was maximal. Five children may be considered; all were examined over an extended experimental period; of these, three were normal controls and had an average total excretion of 0·18, 0·18 and 0·226 gramme *per diem* respectively; a patient with hyperostosis had a total excretion of 0·091 gramme *per diem*, and one, M.R. (previously reported by Hansman and Wilson[29]), had at one stage an excretion of 0·201 gramme *per diem*. No attempt was being made to obtain maximal utilization nor the minimal requirements, so that even some of this excreted calcium may represent excretion of excess, and not the irreducible katabolic minimum.

However, assuming that the average figure, 0·176 gramme *per diem*, represents something of the order of the normal katabolic excretion, we may assume that the minimal total requirements are in the vicinity of 0·28 gramme *per diem*. Sherman,[93] who has probably done most work on this subject, considers that a growing child should receive at least 1·0 gramme of calcium a day as an optimal intake; but from a survey of some 200 diets of normal children of the working and middle classes in Sydney[1] who on such a diet are, from general experience, destined to grow to normal adults, the calcium intake was greatly below 1·0 gramme *per diem*; and we have found that 35% of these apparently normal children have a calcium intake of 0·5 gramme or less *per diem*. It would be an interesting study to reexamine this group in ten or fifteen years. Sherman[93] considers that, if there is calcium lack, the skeleton grows to normal size but is poor in bone salts, and that this difference is made good after growth has ceased.

The requirements for phosphorus cannot be similarly considered, because a large percentage of the ingested phosphorus is needed for metabolic processes other than calcification. Indeed, the needs for calcium, except for the skeleton, are so small—there are only some 8·0 grammes of calcium in an adult apart from the skeleton—and those for phosphorus so great that one speculates whether it is not demand for stored phosphorus and not calcium that gives rise to morbid skeletal conditions. Our work at Prince Alfred Hospital seems to indicate clearly that the problem of phosphorus requirements is more important than that of calcium requirements.

Some General and Somewhat Philosophical Considerations.

We have traversed in brief review various aspects of the problem of calcification. You have probably been thinking, as did previous generations: "What limits the growth and determines the shape of bone?" "How does the diaphysis know when to join with the epiphysis?" "How does the bone cell know how much strength is required and when resorption should cease?" "What determines the architecture and accomplishes the engineering feat that makes bone stronger than cast iron?" "Does environment play the essential part or do the osteoblasts 'think' for themselves?" Both conceptions have staunch advocates. Brash[13] follows Lorrain Smith in thinking that such problems are bound up in an understanding of life itself, for which there will be ultimately a philosophical interpretation, but perhaps as scientists we should say with MacCallum:[57]

> The extreme assumption that the Laws of Physics and Chemistry are inadequate to explain the causation of vital phenomena is, of course, not justifiable, for it postulates that we fully comprehend now all the laws of the physical world.

It is certain from the tissue culture work of Murray and Huxley[56] and of Fell[25] that bones develop their natural shape even when grown *in vitro* quite removed from their natural environment. Appleton (quoted by Brash[13]) has shown that secondary centres of ossification of the greater trochanter will still develop even though the attachment of the *gluteus maximus* had been removed long before the centre was due to appear. Selye[90] (Figure XIII) has shown that if the femur of rats thirteen to fifteen days old is amputated obliquely, proximal to the growth centre of the diaphysis, the jutting fragment will first be resorbed by osteoclastic activity and then a new complete growth cartilage will be formed analogous to that removed. The results of such work led Brash to say that:

> The differentiation of the primary forms of bone are inherent and therefore genetically determined; there is therefore a predetermined basis for the mode of growth of bone and consequently for their general orientation.

On the other hand, Carey, Zeit and McGrath[19] removed the patella from young puppies and joined the quadriceps tendon to the patellar ligament. If free functional activity of the limb was permitted, and then only, a new patella developed from a "differentiation of young connective tissue cells". These authors are strongly opposed to Murray's and Fell's conceptions, and from their experiment considered that bone develops as a result of functional needs. But one could go on indefinitely giving, as it were, knock for knock.

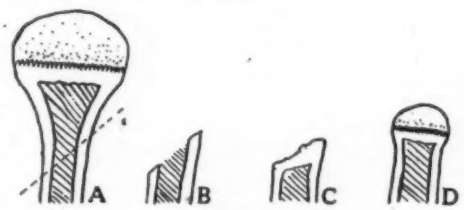

FIGURE XIII B.

Diagram showing formation of new junction cartilage line on an obliquely cut amputation stump. *A* = normal bone (broken line indicates plane of amputation); *B* = stump immediately after amputation; *C* = beginning reconstruction of the stump; *D* = the amputation stump with newly formed regular growth zone, developed in the same plane as the epiphyseal cartilage which has been removed from the original bone. (From Selye.)

For Leriche and Policard (quoted by Brash[13]) and Jones and Roberts[40] the problem of calcification, decalcification and ossification is one of relative vascularity. If the blood supply to a bone is decreased, the bone will undergo increased calcification; if the blood supply increases bone will be resorbed; the decalcification of disuse is explained on the basis of relative hyperæmia. This view is justly opposed by Brash, Keith and Girdlestone. A consideration of the marked vascularity of the site of ossification and of the physiological conception that tissue requirements determine vascularity, and not the contrary, makes it difficult to accept such a theory.

Whatever the truth, we can still feel with Brash[13] "that the substance upon which the stability of the body depends is itself, in its growth, from one point of view, the most plastic of all

[1] A full account of this work is to be published.

tissues; yet from another it is the most stable, so far as the specific form of the bones which it builds is concerned. In nature form and function are the only realities, and substance but their servant." It seems that for us the problem is "how"; for those who follow, "why".

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REFERENCES.

(1) J. C. Aub: "The Harvey Lectures", 1928-1929.
(2) M. Ballin: "Skeletal Pathology of Endocrine Origin", *Annals of Surgery*, Volume XCVIII, 1933, page 868.
(3) D. Barr: "Pathological Calcification", *Physiological Reviews*, Volume XII, 1932, page 593.
(4) H. Bassett: "The Phosphates of Calcium", *The Journal of the Chemical Society*, Volume III, 1917, page 621.
(5) L. H. Behrens and D. P. Barr: "Hyperpituitarism Beginning in Infancy", *Endocrinology*, Volume XVI, 1932, page 120.
(6) R. M. Bethke, C. H. Kick and W. Wilder: "The Effect of the Calcium-Phosphorus Relationship on Growth, Calcification and Blood Composition of Rats", *The Journal of Biological Chemistry*, Volume XCVIII, 1932, page 389.
(7) R. M. Bethke, P. R. Record and D. C. Kennard: "The Comparative Anti-Rachitic Efficiency of Irradiated Ergosterol, Irradiated Yeast and Cod Liver Oil for the Chicken", *The Journal of Nutrition*, Volume VI, 1933, pages 413-425.
(8) C. E. Bills: "The Physiology of the Sterols, including Vitamin *D*", *Physiological Reviews*, Volume XV, 1935, page 98.
(9) A. Bodansky and H. L. Jaffe: "The Production of Osteitis Fibrosa Cystica Generalisata in Guinea-Pigs", *The Journal of Experimental Medicine*, Volume CIII, 1931, page 591.
(10) A. Bodansky and H. L. Jaffe: "Serum Phosphatase", *The Journal of Biological Chemistry*, Volume CV, 1934.
(11) A. Bodansky: "Phosphatase Studies. II: Determination of Serum Phosphatase", *The Journal of Biological Chemistry*, Volume CI, 1933, page 93.
(12) L. J. Bogert and A. B. Hastings: "The Calcium Salts of Bone", *The Journal of Biological Chemistry*, Volume XCIV, 1931, page 473.
(13) J. C. Brash: "Some Problems in the Growth and Developmental Mechanics of Bone", *The Edinburgh Medical Journal*, Volume XLI, 1934, pages 305 and 363.
(14) R. C. Brooke and A. H. Smith: "Inorganic Salts in Nutrition", *The Journal of Biological Chemistry*, Volume C, 1933, page 105.
(15) R. C. Brooke, A. H. Smith and P. H. Smith: "Inorganic Salts in Nutrition: Changes in the Composition of Bone of Rats on Diets Poor in Inorganic Constituents", *The Journal of Biological Chemistry*, Volume CIV, 1934, pages 141-148.
(16) H. B. Brown, A. T. Shohl, E. E. Chapman, C. G. Rose and E. N. Saurwein: "The Effects of Various Levels and Ratios of Calcium to Phosphorus in the Diet upon the Production of Rickets", *The Journal of Biological Chemistry*, Volume XCVIII, 1932, page 207.
(17) Ramon S. Cajal: "Histology" (English translation), 1933.
(18) G. R. Cameron: "The Staining of Calcium", *The Journal of Pathology and Bacteriology*, Volume XXXIII, 1930, page 929.
(19) E. J. Carey, W. Zeit and B. F. McGrath: "Studies on the Dynamics of Histogenesis. XII: The Regeneration of the Patellæ of Dogs", *American Journal of Anatomy*, Volume XL, 1927-1928, page 127.
(20) E. L. Compere: "The Rôle of the Parathyroid Gland in Diseases Associated with Demineralization of the Human Skeleton", *The Journal of Bone and Joint Surgery*, Volume XV, 1933, page 142.
(21) L. R. Dragstedt: "The Physiology of the Parathyroid Gland", *Physiological Reviews*, Volume VII, 1927, page 499.
(22) G. S. Dodds: "Osteoclasts and Cartilage Removal in Endochondral Ossification of Certain Mammals", *American Journal of Anatomy*, 1932, pages 97-127.
(23) M. M. Elliot and E. B. Jackson: "Bone Development of Infants and Young Children in Puerto Rico", *American Journal of Diseases of Children*, Volume XLVI, 1933, pages 1237-1262.
(24) W. Engelbach: "Juvenile Hypopituitarism Treated with Evans' Growth Hormone", *Endocrinology*, Volume XVI, 1932, pages 1-19.
(25) H. B. Feil: "The Histogenesis of Cartilage and Bone in the Long Bones of the Embryonic Fowl", *The Journal of Morphology and Physiology*, Volume XL, 1925, pages 417-460.
(26) M. H. Fischer and M. O. Hooker: "The Lyophilic Colloids (Their Theory and Practice)", 1933.
(27) B. L. Guyatt, H. K. Kay and H. D. Branion: "Beryllium Rickets", *The Journal of Nutrition*, Volume VI, 1933, page 313.
(28) A. Ham: "The Last Hundred Years in the Study of Bone", *The Journal of the American Dental Association*, Volume XXI, 1934, page 3.
(29) F. S. Hansman and F. H. Wilson: "Calcium and Phosphorus Metabolism in Diseases of the Thyreoparathyreoid Apparatus", THE MEDICAL JOURNAL OF AUSTRALIA, January 13 and 20, 1934, pages 37 and 81.
(30) H. A. Harris: "Bone Growth in Health and Disease", 1933.
(31) F. B. Hawk and O. Bergeim: "Practical Physiological Chemistry", Tenth Edition, page 208.
(32) A. F. Hess, F. S. Berliner and M. Weinstock: "Investigation of the Comparatice Ash Content of Metaphyses and Shafts of Bone", *The Journal of Biological Chemistry*, Volume XCIV, 1931, page 9.
(33) L. E. Holt, V. K. La Mer and H. B. Chown: "Studies in Calcification", *The Journal of Biological Chemistry*, Volume LXIV, 1925, pages 509, 567, 579.
(34) J. Howland, W. McKim Marriott and B. Kramer: "Studies upon the Inorganic Composition of Bones", *The Journal of Biological Chemistry*, Volume LXVIII, 1926, page 721.
(35) C. B. Huggins: "The Phosphatase Activity of Transplants of the Epithelium of the Urinary Bladder to the Abdominal Wall producing Heterotopic Ossification", *The Biochemical Journal*, Volume XXV, 1931, page 728.
(36) D. Hunter: "Critical Review: The Metabolism of Calcium and Phosphorus and the Parathyroids in Health and Disease", *The Quarterly Journal of Medicine*, Volume XXIV, 1931, page 393.
(37) N. W. Ingalls: "Observations on Bone Weight", *American Journal of Anatomy*, Volume XLVIII, 1931, page 45.
(38) H. D. Jenner and H. D. Kay: "Bone Phosphatase", *The British Journal of Experimental Pathology*, Volume XIII, 1932, page 22.
(39) J. H. Jones, M. Rapaport and H. L. Hodes: "The Source of Excess Calcium in Hypercalcæmia Induced by Irradiated Ergosterol", *The Journal of Biological Chemistry*, Volume LXXXIX, 1930, page 647.
(40) R. W. Jones and R. E. Roberts: "Calcification, Decalcification and Ossification", *The British Journal of Surgery*, Volume XXI, 1934, page 461.
(41) H. D. Kay and B. L. Guyatt: "Experimental Rickets as a Phosphorus Deficiency Disease", *Nature*, Volume CXXXI, 1933, page 468.
(42) H. D. Kay: "Phosphatase in Growth and Disease of Bone", *Physiological Reviews*, Volume XII, 1933, page 384.
(43) A. Keith: "Studies of the Anatomical Changes that Accompany Certain Growth Disorders of the Human Body", *The Journal of Anatomy*, Volume LIV, 1920, page 101.
(44) A. Keith: "Menders of the Maimed", 1919.
(45) S. W. F. Klatzien, V. Templin, H. Steenbock and B. H. Thomas: "Vitamin *D* and the Conservation of Calcium in the Adult", *The Journal of Biological Chemistry*, Volume XCVII, 1933, page 265.
(46) B. Kramer and M. J. Shear: "The Composition of Bone. IV: Primary Calcification", *The Journal of Biological Chemistry*, Volume XCIX, 1928, page 147.
(47) B. Kramer, M. J. Shear and J. Siegel: "The Composition of Bone. X: Mechanism of Healing in Low-Phosphorus Rickets", *The Journal of Biological Chemistry*, Volume XCI, 1931, page 271.
(48) G. Lusk: "The Science of Nutrition", 1928, page 535.
(49) A. A. Maximow and W. Bloom: "Textbook of Histology", Second Edition, 1934.
(50) J. P. Maxwell: "Further Studies in Adult Rickets (Osteomalacia) and Fœtal Rickets", *Proceedings of the Royal Society of Medicine*, Section of Obstetrics and Gynæcology, Volume XXVIII, Number 3, 1935, page 265.
(51) A. F. Morgan: "The Effect of Diet in Response to Parathyroid Extract and Vitamin *D* Diets on Normal Calcium, Normal Phosphorus Content in Dogs", *American Journal of Physiology*, Volume CV, 1933, pages 621-634.
(52) A. F. Morgan: "The Effect of High Calcium, Low Phosphorus Diet in Dogs", *American Journal of Physiology*, Volume CV, 1933, pages 596-607.
(53) A. F. Morgan, E. A. Garrison and M. J. Hill: "The Effect of Low Calcium, High Phosphorus Diet in Dogs", *American Journal of Physiology*, Volume CV, 1933, pages 608-620.
(54) A. F. Morgan and J. G. Field: "The Relation of Calcium and Phosphorus of Diet to Response of Parathyroid Extract in Rats", *American Journal of Physiology*, Volume CV, 1933, pages 585-595.
(55) S. Morgulis: "Studies on the Chemical Composition of Bone Ash", *The Journal of Biological Chemistry*, Volume XCIII, 1931, page 455.
(56) P. D. F. Murray and J. Huxley: "Self-Differentiation in the Grafted Limb-Bud of Chicks", *The Journal of Anatomy*, Volume LIX, 1925, page 379.
(57) McCallum (quoted from Burns): "An Introduction to Biophysics", Second Edition.
(58) F. C. McLean and A. B. Hastings: "The State of Calcium in the Fluids of the Body", *The Journal of Biological Chemistry*, Volume CVIII, 1935, page 285.
(59) W. M. Neal, L. S. Palmer, C. H. Eckles and J. W. Gullickson: "The Effect of Age and Nutrition on the Calcium Phosphate/Calcium Carbonate Ratio in the Bones of Cattle", *The Journal of Agricultural Research*, Volume XLII, 1931, page 115.

(60) Needham: "Chemical Embryology", Volume III, 1931.
(61) L. I. Pugsley and E. Anderson: "The Effect of Desiccated Thyroid, Irradiated Ergosterol and Ammonium Chloride on the Excretion of Calcium in Rats", *The Biochemical Journal*, Volume XXVIII, 1934, page 754.
(62) L. I. Pugsley and E. Anderson: "The Effect of the Administration of Calciferol on the Increased Calcium Excretion Induced by Thyroxine", *The Biochemical Journal*, Volume XXVIII, 1934, page 1313.
(63) L. I. Pugsley and H. Selye: "The Histological Changes in the Bone Responsible for the Action of Parathyroid Hormone on the Calcium Metabolism of the Rat", *The Journal of Physiology*, Volume LXXIX, 1933, page 113.
(64) C. I. Reed, E. A. Thacker, L. M. Dillman and J. W. Welch: "The Effect of Irradiated Ergosterol on the Metabolism of Normal Dogs", *The Journal of Nutrition*, Volume VI, 1933, page 355.
(65) C. I. Reed, L. M. Dillman, E. A. Thacker and R. I. Klein: "The Calcification of Tissues by Excessive Doses of Irradiated Ergosterol", *The Journal of Nutrition*, Volume VI, 1933, page 371.
(66) W. M. Roberts: "Variations in Phosphatase Activity of Blood in Disease", *The British Journal of Experimental Pathology*, Volume XI, 1930, page 90.
(67) R. Robison: "The Possible Significance of Hexose-Phosphoric Esters in Ossification", *The Biochemical Journal*, Volume XVII, 1923, page 286.
(68) R. Robison and K. M. Soames: *Ibidem*, Volume XVIII, 1924, page 740.
(69) H. D. Kay and R. Robison: *Ibidem*, Volume XVIII, 1924, page 755.
(70) H. W. Goodwin and R. Robison: *Ibidem*, Volume XVIII, 1924, page 1161.
(71) M. Martland and R. Robison: *Ibidem*, Volume XVIII, 1924, page 1354.
(72) R. Robison: *Ibidem*, Volume XX, 1926, page 388.
(73) M. Martland and R. Robison: *Ibidem*, Volume XX, 1926, page 847.
(74) M. Martland and R. Robison: *Ibidem*, Volume XXI, 1927, page 665.
(75) R. Robison and K. M. Soames: *Ibidem*, Volume XXIV, 1930, page 1922.
(76) R. Robison, M. MacLeod and A. H. Rosenheim: *Ibidem*, Volume XXIV, 1930, page 1927.
(77) M. Martland and R. Robison: "The Preparation and Use of the Bone Phosphatase", *Ibidem*, Volume XXIII, 1929, page 237.
(78) M. Martland, F. S. Hansman and R. Robison: "The Phosphoric Esterase of Blood", *ibidem*, Volume XVIII, 1924, page 1152.
(79) H. B. Fell and R. Robison: "The Development and Phosphatase Activity In Vivo and In Vitro of the Mandibular Skeletal Tissue of the Embryonic Fowl", *ibidem*, Volume XXIV, 1930, page 1905.
(80) R. Robison and A. H. Rosenheim: "The Calcification of Hypertrophic Cartilage In Vitro", *ibidem*, Volume XXVIII, 1934, page 684.
(81) A. H. Rosenheim and R. Robison: "The Calcification In Vitro of Kidney, Lung and Aorta", *ibidem*, Volume XXVIII, 1934, page 712.
(82) A. H. Rosenheim: "The Effect of Serum-Proteins on Calcification In Vitro", *ibidem*, Volume XXVIII, 1934, page 699.
(83) A. H. Rosenheim: "Variability in the Activity of the Calcifying Mechanism in the Bones of Rachitic Rats", *ibidem*, Volume XXVIII, 1934, page 708.
(84) M. G. Macfarlane, L. M. B. Patterson and R. Robison: "The Phosphatase Activity of Animal Tissues", *ibidem*, Volume XXVIII, 1934, page 720.
(85) J. S. F. Niven and R. Robison: "The Development of the Calcifying Mechanism in the Long Bones of the Rabbit", *ibidem*, Volume XXVIII, 1934, page 2237.
(86) H. B. Fell and R. Robison: "The Development of the Calcifying Mechanism in Avian Cartilage and Osteoid Tissue", *ibidem*, Volume XXVIII, 1934, page 2243.
(87) R. Robison: "The Significance of Phosphoric Esters in Metabolism", 1932.
(88) H. H. Rosebury, H. B. Hastings and J. K. Morse: "X-Ray Analysis of Bones and Teeth", *The Journal of Biological Chemistry*, Volume XC, 1931, page 395.
(89) L. G. Rowntree, J. H. Clark and A. M. Hanson: "The Biologic Effect of Thymus Extract (Hanson)", *The Journal of the American Medical Association*, Volume CIII, 1934, page 1425.
(90) H. Selye: "The Mechanism Controlling Growth in Length of the Long Bones", *The Journal of Anatomy*, Volume LXVIII, 1934, page 289.
(91) J. Sendroy and A. B. Hastings: "Studies of Solubility of Calcium Salts: Solubility of Calcium Carbonate and Tertiary Calcium Phosphate under Various Conditions", *The Journal of Biological Chemistry*, Volume LXXI, 1926-1927, page 797.
(92) D. H. Shelling, D. E. Asher and D. A. Jackson: "Calcium and Phosphorus Studies", *Bulletin of the Johns Hopkins Hospital*, Volume LIII, 1933, page 348.
(93) H. C. Sherman: "The Chemistry of Food and Nutrition", Fourth Edition, 1933.
(94) H. C. Sherman and E. J. Quinn: "The Phosphorus Content of the Body in Relation to Age, Growth and Food", *The Journal of Biological Chemistry*, Volume LXVII, 1926, page 667.
(95) H. C. Sherman and L. E. Booher: "The Calcium Content of the Body in Relation to that of the Food", *ibidem*, Volume XCIII, 1931, page 93.
(96) P. G. Shipley, B. Kramer and J. Howland: "Studies upon Calcification In Vitro", *The Biochemical Journal*, Volume XX, 1926, page 379.
(97) A. T. Shohl, H. B. Brown, E. E. Chapman, C. Rose and E. M. Saurwein: "The Evaluation of the Phosphorus Deficiency of the Rickets-Producing Diet", *The Journal of Nutrition*, Volume VI, 1933, page 271.
(98) A. H. Shohl: "Rickets and Tetany due to Low Calcium Diets", *The Proceedings of the American Society of Biological Chemistry*, Volume LXXXV, 1935.
(99) A. T. Shohl, H. B. Brown, E. E. Chapman, C. S. Rose and E. M. Saurwein: "A Diet which Demonstrates the Effect of the Acid-Base Content upon the Production of Rickets and also Causes Idiopathic Tetany", *The Journal of Biological Chemistry*, Volume XCVIII, 1932, page 215.
(100) A. E. Sobel, A. R. Goldfarb and B. Kramer: "Studies of Incurable Rickets. II: Rôle of the 'Local Factor' and of Viosterol in the Pathogenesis of Rickets due to Beryllium", *ibidem*, Volume CVIII, 1935, page 395.
(101) Jean Smith and M. Maizels: "The Plasma Phosphatase in Rickets and Scurvy", *Archives of Diseases in Childhood*, Volume VII, 1932, page 149.
(102) Jean Smith: "Plasma Phosphatase in Rickets and other Disorders of Growth", *ibidem*, Volume VIII, 1933, page 215.
(103) H. Steenbock, J. W. F. Klatzien and J. G. Halpin: "The Reaction of the Chicken to Irradiated Ergosterol and Irradiated Yeast as Contrasted with the Natural Vitamin *D* of Fish-Liver Oils", *The Journal of Biological Chemistry*, Volume XCVII, 1932, page 249.
(104) C. Witherington Stump: "The Histogenesis of Bone", *The Journal of Anatomy*, Volume LIX, Part II, 1924-1925, page 137.
(105) *"Tabellæ Biologicæ"*, Volume III, 1926.
(106) N. W. Taylor and C. Sheard: "Microscopic and X-Ray Investigations of the Calcification of Tissue", *The Journal of Biological Chemistry*, Volume LXXXI, 1929, page 478.
(107) A. B. Taylor, C. B. Weld, H. D. Branion and H. D. Kay: "A Study of the Action of Irradiated Ergosterol and of its Relationship to Parathyroid Function", *Canadian Medical Association Journal*, Volume XXIV, 1931, page 763, and Volume XXV, 1931, page 20.
(108) A. Theiler: "The Osteodystrophic Diseases of Domesticated Animals", *The Veterinary Journal*, Volume IV, 1934, page 143, and Volume V, 1934, page 183.
(109) V. M. Templin and H. Steenbock: "Vitamin *D* and the Conservation of Calcium in the Adult. II: The Effect of Vitamin *D* on Calcium Conservation in *Adult* Rats Maintained on Low Calcium Diets", *The Journal of Biological Chemistry*, Volume C, 1933, page 209.
(110) D. L. Thomson and J. B. Collip: "The Physiology of the Parathyroid Glands", *Physiological Reviews*, Volume XII, 1932, page 309.
(111) M. L. Washburn and M. J. Shear: "The Composition of Bone: Direct Gravimetric Determination", *The Journal of Biological Chemistry*, Volume XCIV, 1932, page 21.

ON HERPES, CRAMPS, FIDGETS AND OTHER DISORDERED SENSATIONS.

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Sydney.

I DARE say this trifling paper may provoke a smile from my younger, but, I hope, tolerant, readers. Possibly they may have a satisfying explanation for all the small aberrant clinical facts which I mention, but I admit without much shame that I cannot myself explain some of them in a way to satisfy my own mind.

Some years ago a writer, I think in a leading article in *The British Medical Journal*, asked the question: "Do we, as doctors, know the cause of every fleeting pain, spasm and passing disorder of sensation which may occur to most of us almost every day of our lives?" We do not. If we are wholesome, normal-minded folk, we dismiss them from our thoughts and these dysæsthesiæ are no more felt, till next time, when we say: "Oh, there it is again; it means nothing." Not so if we are of the introspective, ultra-neurotic or "tommyrotic" constitution. Such people dwell on their somatic sensations, encourage lines of abnormal centripetal messages, and thus may establish hypochondria and hysteria and professional invalidisms. Please do

not think I am holding up the neurotic to disdain. If, indeed, a neurotic is often a person who is unable to strike a sensible bargain with existence, at least some of these neurotics are the salt of the earth, even if difficult. Nevertheless, both these passing paræsthesiæ and dysæsthesiæ, which are mostly just subjective symptoms, as well as other manifestations which reach the dignity of objective signs, such as herpes, are often hard to explain and are not without interest to the clinician.

There are two types of herpes. They are diverse. Let us consider *herpes zoster*. The laity know it well by the name of shingles, which strictly really connotes only its thoracic distribution, for shingles is a corruption of the Latin word *cingulum*, a belt or girdle; but, as we know, it has other seats of election, although it does not, I think, ever appear distal to the knee or elbow. *Herpes zoster* is a good example of the peripheral projection of pain.

Hippocrates said the prognosis was good so long as it did not encircle, but fatal if it did so. But it never did become bilateral, so all the patients got well, although post-herpetic neuralgia may so persist in the aged and be so immedicable that suicide in some cases has seemed the only way out of misery.

Most writers mention the correct fact that a second attack never occurs. This, however, is not absolutely true, for many years ago I attended a woman of over forty, in her second confinement, eighteen years after her first and only *accouchement*. She had scars of a severe *herpes frontalis* on her right brow. During this second puerperium another attack of herpes took place over exactly the same area as on the first occasion. This second attack was therefore a remarkable exception to the general rule, and still more so because of the association with child-bearing and recurrence over the same nerve area.

Quite a lot of work has been done regarding herpes, both zoster and labial. Certainly *herpes labialis* is distinct from *herpes zoster* and varicella. It has been suggested, however, that varicella may sometimes take on a neurotrophic tendency and invade the posterior root ganglia and so cause neurotrophic ulcers. No virus has been obtained from such ulcer, hence some observers have thought that the virus of varicella and *herpes zoster* are the same. The skin lesions of *herpes zoster* are trophic and have no virus in them. The virus is situated in the posterior root ganglia. The whole subject is not yet clear and is controversial. I always think of the ordinary inflammation of the posterior root ganglia in *herpes zoster* as analogous to the lesion in the anterior cornua, with its often tragic consequences to children so affected. *Herpes labialis* is a strange affection. It is believed to be due to a distinct virus, as I said, different to that of *herpes zoster* or varicella. It differs from *herpes zoster* in that one attack confers no immunity from subsequent outbreaks. In most virus diseases one attack does confer immunity — I have already referred to the usual immunity in *herpes zoster*. Normally the virus of *herpes labialis* is dermotrophic—the virus is in the vesicles—but it may become neurotropic by animal passage. Sometimes it is noted that in a family one member develops varicella while another has *herpes zoster*. As to cerebro-spinal meningitis, that is a bacterial disease, and no meningitis is due to a virus. That encephalitis is due to the virus of *herpes labialis* is claimed by some people, but, as far as I know, that has by no means been proved. I owe the references to these points to the kindness of Dr. Keith Inglis and Dr. H. K. Ward, who looked into the matter on my behalf.

One should remember that muco-cutaneous areas, such as the lips and nose, are not its only sites. The penis and vaginal orifice are quite commonly affected, and I have been told by various trepidant patients of both sexes that their attack came on shortly after intercourse, to their great alarm. Herpes of the prepuce and *glans penis* is not very painful. I believe this is due to the *glans penis* being curiously insensitive to ordinary tactile sensation, however sensitive it may be to the special stimulus of sexual contact.

Another less common site is the pharynx. Here it is intensely painful, as I well know. It may alternate with the preputial or vaginal manifestations, and I have known this sequence to run in a family. Morell Mackenzie described it fully over fifty years ago, but the earliest account was by the great Trousseau. He said that it was most often seen during epidemics of diphtheria, and the shallow ulcers of the herpes became themselves infected by the diphtheritic process. Trousseau's paper is buried in the Sydenham Society's Transactions, which are less read than they deserve. I regarded herpes of the pharynx then, as I still do, as similar to *herpes labialis*, and not of the same nature as *herpes zoster*. That the presence of *herpes labialis* is of favourable prognostic import in pneumonia is possibly true, yet I have myself seen pneumonia patients die with florid herpes on their nasal and labial regions. I associate the efflorescence of herpes of the lips and skin over the submental region with chills, over-fatigue, missing a meal and a long fast. Possibly some gastro-intestinal disturbance—something eaten that disagrees—all common incidents of the domestic day. When I have an attack I get some shivering and feel seedy, and almost at once am conscious of a hot, itchy smarting at the affected area, with some small papules to be felt. Painting these parts with rectified spirits and smearing on some "Hazeline cream" relieve the discomfort.

You are all probably familiar with people who have odd patches of whitish hair in beard, moustache or scalp. These differences of colour may be due to various causes interfering with the trophic processes of hair growth and pigmentation, vascular or neural. Occasionally you may come across a patient with a curious tuft of blanched hair in the beard over the mental foramen. (I may here interpolate the caution that the man must be growing a

ILLUSTRATIONS TO THE ARTICLE BY DR. F. S. HANSMAN.

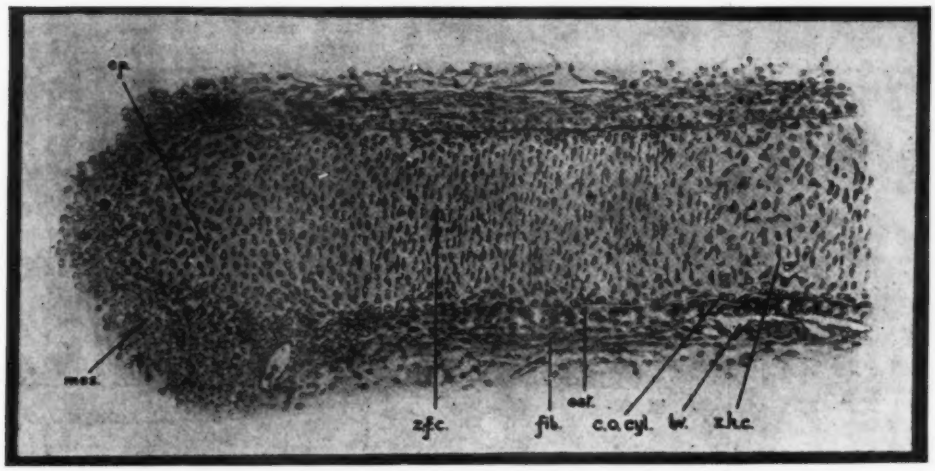

FIGURE I.

Rudiments of limb bone of chick. b.v. = blood vessel; c.o.cyl. = central osseous cylinder (primitive sheath of bone); ep. = epiphysis; fib. = fibrous layer of periosteum; mes. = undifferentiated mesenchyme; ost. = osteoblastic layer of periosteum; z.f.c. = zone of flattened cells just beyond convexity of ellipse; z.h.c. = zone of hypertrophied cartilage cells in centre of ellipse. (From Fell.)

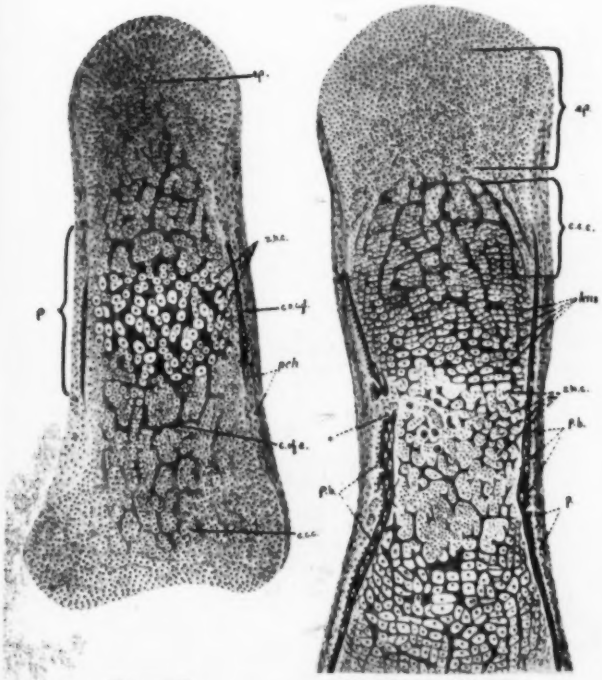

FIGURE II. FIGURE III.

(From Maximow and Bloom.)

Human phalanges, three months human fœtus. (Legend somewhat modified.) c.c.c. = columns of cartilage cells; c.o.cyl. = central osseous cylinder; c. of e. = convexity of ellipse; ep. = epiphysis; P. = periosteum; p.b. = periosteal bone; pch. = perichondrium; z.c.c. = zone of calcifying cartilage; z.h.c. = zone of hypertrophic cartilage cells; * = invasion of osteogenic mesenchyme into diaphysis.

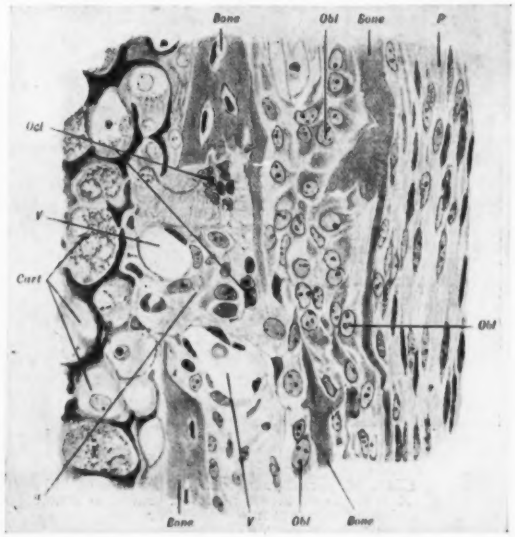

FIGURE IV.

a. = a bud of multipotential mesenchyme penetrating the periosteal sheath of bone to invade the cartilage; obl. = osteoblasts; ocl. = osteoclasts; p. = periosteum; v. = blood vessels. (From Maximow and Bloom.)

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FIGURE VII.
Cross-section of human hip bone in polarized light. The cross-sections of three Haversian systems are seen as bright Maltese crosses. × 130. (Redrawn from Gebhardt. From Maximow and Bloom.)

FIGURE XI.
Showing effect of parathyreoid medication on calcification in rats. *A* = control, stock diet; *B* and *C* = stock diet and 10 units parathormone daily for twenty-one and fourteen days respectively. Rat *B* was twenty-four days and rat *C* was eighteen days old when injections were begun. Notice the extreme degree of trabeculation, especially in *C*, as contrasted with the control; the slight amount of fibrosis (arrow) between the uppermost trabeculæ and also the distance between the cartilaginous zone and the marrow cavity. (From Shelling, Asher and Jackson.)

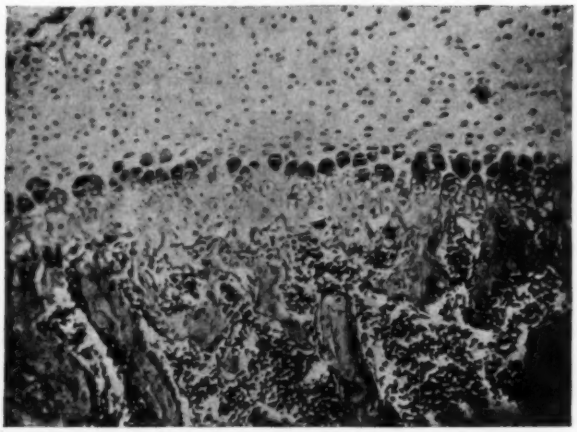

FIGURE XIIIA.
Amputation stump nineteen days after operation, showing newly formed typical growth cartilage line. (From Selye.)

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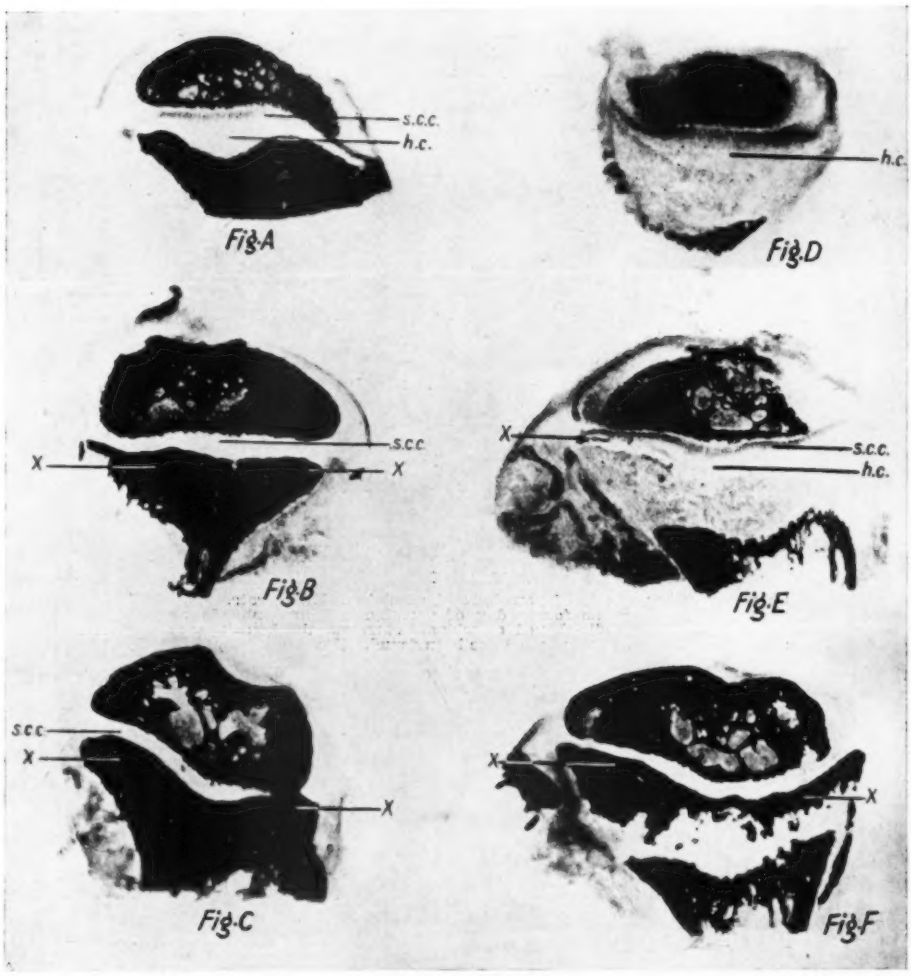

FIGURE X.

Calcification of slices of rhachitic bones (tibiæ) of rats. *In vitro* specimens stained by Kossa's silver nitrate method. *A*, *B* and *C* are all from one animal which had been on a rhachitogenic diet for ten days. *A* = control slice. Note narrow zone of uncalcified hypertrophic cartilage. *B* = slice after immersion for twenty hours at 37° C. and pH 7·4 in an inorganic solution consisting of 8·0 milligrammes of calcium and 4·0 milligrammes of inorganic phosphate per 100 cubic centimetres of basal salt solution. *C* = slice after immersion for twenty hours in a solution containing organic phosphate in addition, that is, 8·0 milligrammes of calcium, 3·0 milligrammes of inorganic phosphate and 10·0 milligrammes of organic phosphate per 100 cubic centimetres. *D*, *E* and *F* are all from one animal, which had been on a rhachitogenic diet for twenty-eight days. *D* = control slice. Note breadth of uncalcified zone. *E* = slice after twenty hours in a solution of the same composition as in *B*. Note very small amount of new calcification obtained *in vitro*, indicating the decreased calcifying power of the hypertrophic cartilage. Note deposit on the line (*X* in diagram). *F* = slice after twenty hours in a solution of the same composition as in *C*. Calcification is denser and more extensive than in absence of phosphoric ester, but does not extend to shaft. *s.c.c.* = small-celled cartilage; *h.c.* = hypertrophied cartilage. (From Rosenheim.)

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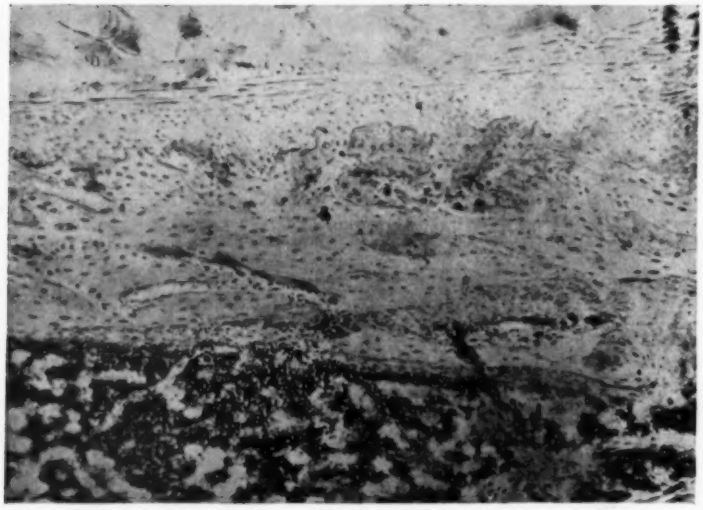

FIGURE XIIA.

Showing further effects of parathyreoid administration in rats. Histological picture of bone on the fourth day of parathyreoid hormone administration. Thick layers of spindle-shaped osteoblasts surround the bone tissue; at the same time numerous osteoclasts have been found. (From Pugsley and Selye.)

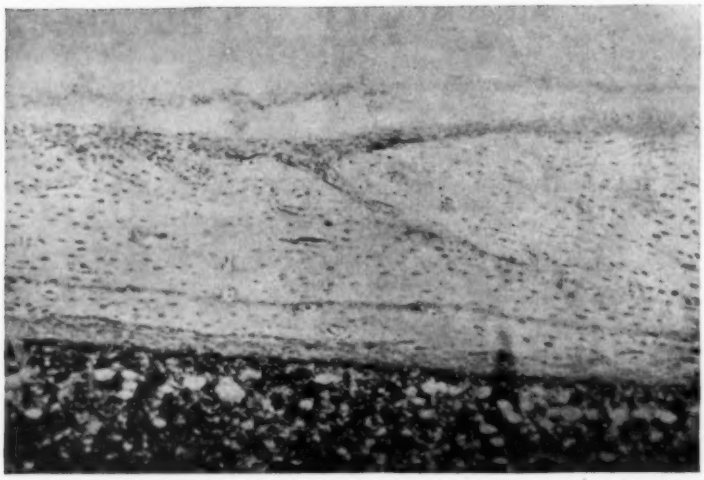

FIGURE XIIB.

Showing further effects of parathyreoid administration in rats. Histological picture of bone at the eleventh day of parathyreoid administration. The osteoclasts have disappeared and only osteoblasts can be seen. (From Pugsley and Selye.)

beard at the time!) When I was a dresser under Mr. Joseph Bell, where Arthur Conan Doyle and David Orme Masson, of Melbourne, were my fellow students, Joe Bell, after whom Sherlock Holmes was taken, was holding one of his wonderful out-patient clinics. One day a man came in with a white patch over his right mental foramen. Bell looked at him and said: "My man, is your right stone far smaller than your left?" "Yes", said the astonished patient. On examination his right testicle was found to be atrophied. The class gaped; Bell had no explanation to offer, nor have I now. The man, so far as I remember, had not had mumps. You cannot see such cases often, even in a long lifetime of practice, and you cannot always ask those you do about the size of their testes. I have, however, done so on two or three occasions, and I have confirmed Bell's observation, but not invariably. Hence I do not believe that this strange association is constant.

I wonder if we realize how miserable patients may be made by cramps and fidgets when these unwished and uncontrolled muscular contractions, local or in groups, continue for any length of time. Annoying as they are in presumably fairly healthy people, think of the extra woe they must be to people with broken legs nicely done up in splints! I regard them as first cousins, for the same conditions may often cause both. I do not know of any perfectly satisfying explanation being given of their ætiology, but certain things make their appearance probable. Cramps, when severe, are really quite formidable troubles; occurring in certain circumstances they well may be embarrassing and sometimes even dangerous.

Years ago everybody who died in the water was supposed to have had cramp—usually of the heart, said the coroner. I do not deny the possibility of cramp causing death by drowning in several easily understood ways; but, for my part, I have long believed that heart failure of several kinds would account for these watery deaths. Cramps are not uncommon in grave food poisoning, and I think in less severe forms of food toxæmia both cramp and fidgets may occur. Exposure to cold may certainly cause the former, and likewise getting in or out of some strained position where muscles are over-contracted or irritated. I have no doubt that any pathological change in the vascular supply of the region affected may be the cause, as, say, diabetics, where, too, these patients are also often dehydrated.

Men tell me that suspenders for stockings and tight garters are capable of starting cramps. I am sure they are made more likely by prolonged violent exertion and profuse sweating, whereby the body is dehydrated and the blood stream is carrying more than its usual amount of the products of tissue metabolism. I shall have more to say possibly on this point. In cholera, how frequent are cramps, probably due partly to dehydration from the colliquative diarrhœa of that disease. The opposite conditions, of too little exercise and sluggish bowels, may lead to fidgets from lack of movement of the fluids in the vascular and lymphatic systems. In such cases massage does good.

Fidgets, out of bed, are dependent on psychical conditions as well as physical. Sitting on an uncomfortable chair in a cold and stuffy room and bored stiff with your company, you are just the *milieu* to find yourself with them. I have even known them to occur in a church. In bed matters are still worse. They banish sleep and I do not doubt that they must sometimes be an active source of connubial unrest. I dare say the same causes which produce cramps in one person may lead to fidgets in another; but some fidgets are certainly related to constitutional states and food, for I have seen gouty subjects who had sleep-killing fidgets relieved by colchicum and lithia.

Alkalis in some cases act well. Cramps, I am told, may be mitigated by doses of aspirin. Again and again a hot bath immediately before going to bed has promoted untroubled sleep for a number of hours. I am sure that most cases of fidgets, and perhaps cramps also, in bed may be relieved by getting up, emptying the bladder, walking about the room, rubbing the affected part, but, above all else, swallowing some fluid or a little food. Some hot agreeable liquid is best, but even cold water may suffice. I am afraid that what I have said is quite in the style of the empirical medicine and pathology of the eighteenth century, but nevertheless whatever be the physiological explanation of these things, the suggestions I have made for their relief are, I do know, of some practical benefit. When one thinks of the action of these salutary measures one cannot help believing that the causation of cramps and fidgets is partly chemical—a failure in the metabolism of nitrogenous waste, or a toxæmia from bacterial products.

These are merely my crude ideas of their causation, for I am ignorant of any better explanation of them. Indeed Professor Priestley tells me that he knows of no special work dealing with a physiological interpretation of their recurrence.

But there is one special manifestation of cramp about which I am reminded by Dr. J. C. Storey, namely, the so-called "miner's cramp", and which some of you may have seen in firemen in the Red Sea, or indeed in any conditions where men labour in great heat, with profuse sweating, with the consequent thirst and its assuagement by vast draughts of plain water. I find quite a respectable amount of literature on this special form of cramp. Its best presentment is not in a book of medicine by a medical man, but in that delightful and suggestive volume by J. B. S. Haldane, called "Possible Worlds". In a chapter devoted to "Water and Salt Poisoning" he tells us the story of these violent cramps met with in mines. I do not think I can do better than quote some paragraphs from this book:

> Perhaps the hottest place in England is about a mile underground in a well-known Lancashire coal-pit, where the miners work in boots and bathing drawers and empty the sweat from their boots at lunch. One man sweated eighteen pounds in the course of a shift, and it is probable

that even this figure has been exceeded. This sweat contained about an ounce of salt—twice what the average man consumes in all forms per day. The salt loss was instinctively made up above ground by means of bacon, kippers, salted beer and the like. And as long as they did not drink more than a quart of water underground no harm came to the miners. But a man who has sweated nearly two gallons is thirsty, and coal-dust dries the throat, so this amount was often exceeded and the excess occasionally led to appalling attacks of cramp, often in the stomach, but sometimes in the limbs or back. The victims had taken more water than was needed to adjust the salt concentration in their blood, and the diversion of blood from their kidneys to their muscles and skin was so great that they were unable to excrete the excess. The miners in question were offered a solution of salt in water, which was of about the composition of sweat and would be somewhat unappetizing to the average man. They drank it by quarts and asked for more. And now that it has become their regular beverage underground there is no more cramp and far less fatigue. It is almost certain that the cramp of stokers and of iron and glass workers, which is known to be due to excessive water drinking, could be prevented in the same way.

Dr. Brockbank (*The British Medical Journal*, January 22, 1929) describes a case in point and gives a number of references, among others one by K. N. Moss, Professor of Coal Mining in the University of Birmingham, which deals with the subject.

"In severe cases it may take six men to hold down a sufferer and straighten out the affected limb." Haldane took the view that the cramp might depend on excessive loss of chlorides by continued sweating. The matter was investigated.

A sample of urine obtained by a miner who was subject to these cramps, at the end of a shift, gave not the slightest cloudiness with nitrate of silver, though only five cubic centimetres were secreted in four and a half hours. This great shortage of chlorides in the urine must have been brought about by a combination of excessive sweating and drinking of water. Sweating by itself could hardly have had this effect, as sweat only contains 0·2 per cent. of chloride, and sweating by itself would tend to concentrate the chlorides in the blood plasma.

We may therefore regard these special kinds of cramp as a water poisoning, and they can be avoided by giving the men exposed to the causative conditions a drink containing just sufficient salt to balance the loss of salt by sweating. One point in the diagnosis of such cases is worth remembering, namely, the error of mistaking an extreme case of cramp, say in a fireman, for heat stroke has occasionally been made. The chief point to rely on is that in heat stroke one looks for pyrexia, whereas in cramps the temperature is probably subnormal.

I think we do not sufficiently read the thoughts of old writers in medicine. They had neither our later knowledge nor our instruments of precision, yet they were incredibly shrewd observers and correct "deducers", and it is not difficult to pick out gems of wisdom from their works. Here is one from Bacon, not a doctor, but one "who made all knowledge his province". I often quote him. He tells us that "it is good for old men to eat nitre". Why? Because the nitrate of Elizabethan times was impure and contained plenty of nitrite, and so no doubt may have slackened the arteries of the hyperpietic old gentlemen of those "spacious days". That cramps and fidgets should be due to some toxic abnormality in the blood stream is no more surprising than the presence of myoidema in a tuberculous patient, with his particular toxin running in his vessels and making his muscle fibres unduly sensitive to the external stimulus of a tap. I do not know if myoidema connotes anything more than "the irritability of exhaustion", whatever that may mean.

You may meet, occasionally, people who possess patches of skin, most often on the upper parts of the thigh or about the knee, with a disordered condition of sensation. A light touch on these areas is unfelt, but firm pressure, say in kneeling, if the area be near the patella, evokes a curious painful burning sensation. I should describe it as akin to an *anæsthesia dolorosa*, but not the dissociated paræsthesia of syringomyelia. I am ignorant of any explanation of this condition. Tactile sensation of the skin of the lower part of the thigh, above the knee, is often, I admit, somewhat curiously blunted in many people. It is also the region where anæsthetic patches in nerve leprosy are often found and may be easily demonstrated.

I was doing this years ago for my class and had smartly tapped the leg with a suitably sharp-pointed instrument. Blood was visible, yet the patient made no sign. "Oh", said one of the class, a bright spark of everlasting cocksureness, "I don't think that very unusual, I would myself hardly feel it at all." With that, he smartly jabbed the same instrument, unsterilized, into his thigh through his trousers. I suppose the cloth acted as a protection. I was overcome with rage and fear, and I mentioned what I thought of his deed. Anyway, an ellipse of tissue surrounding the puncture he had made was promptly excised; so far as I know, he had no bad result from his folly.

When James Mackenzie wrote his first and best book on heart disease, it profoundly influenced medical opinion in cardiology. It was doubly to his credit that he accumulated the material for so doing during his formative years as a general practitioner in the soul-deadening town of Burnley, but he is less well known for his work on pain, in collaboration, I think, with Head. That also was most suggestive, and explained many obscure and aberrant symptoms. A familiarity with the peripheral projection of pain, which it teaches, is of great value to the clinician. In gall-bladder disease there is a small point worth mentioning, which I have noticed and pointed out elsewhere, namely, that often over the skin of the xiphisternum there is intense sensitiveness to touch and a burning sensation is complained of on pressure.

Professor Jones, of Dunedin, in an admirable paper dealing with such points, lays stress on the place of tenderness being just close to the costal cartilage of the right side. I imagine his point of pain and mine are expressions of the same condition of nerve conduction from the same peccant region. Although, as I said, most queer passing pains in different parts of the body, usually superficially situated, are of no clinical importance, yet there are others which will readily occur to our

minds, are of real diagnostic or prognostic value and are examples of peripheral projection of pain. I recall several: testicular pain in renal calculus, knee pain in early hip joint affection, misleading abdominal pain in an acute inflammatory lesion within the thorax, penile pain from trouble at the neck of the bladder, umbilical pain in strangulated inguinal or femoral hernia, numbness of the little finger and half the ring finger when the ulnar nerve is irritated at the elbow. I have already referred to the pains of *herpes zoster*. One ought always to be on the look-out for such referred pains.

I realize that a paper like this, made up of trifles, must be dull to those who read in this journal communications dealing with the results of new treatments, strange maladies and interesting surgical adventures. Still, such trifles loom large in the minds of patients, and it is well that they should sometimes be discussed by those who treat them.

THE GROWTH CURVE OF AUSTRALIAN INFANTS DURING THE SECOND YEAR OF AGE.

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THE baby health centres of New South Wales were established with the object of supervising the development and welfare of infants during the first year of life. As would be natural in such circumstances, some mothers continue to visit the clinics with their babies even after the first birthday, a custom that has been encouraged.

The occasional appearance of an older infant created the demand for a weight chart extending beyond the first birthday. Before such a chart could be constructed weights had to be collected by the sisters of the clinics. In pursuit of this object a campaign was launched in 1933 under the guidance of Dr. Sydney Morris, Director-General of Health, New South Wales; mothers were encouraged to bring the older children to clinics at regular intervals so that the weights might be regularly recorded.

The original intention was to prepare a graph to the third birthday, but unfortunately the numbers available beyond the twenty-fourth month were insufficient to produce a satisfactory curve.

The Material.

By the courtesy of Dr. Morris, weight cards were obtained from almost all the metropolitan centres as well as from several country clinics. In all, 367 cards were selected for analysis, 172 females and 195 males supplying over 4,000 observations.

An analysis was made of the fortnightly weighing in the preparation of the first year curve,[1] but in this series the analysis was confined to the monthly weights. The method was similar to that used in previous papers.

The Results.

The results obtained are shown in Table I, where the number of observations and the mean weight, together with the probable error, are depicted for each month.

TABLE I.

Age in Months.	Males.		Females.		Combined.	
	Number of Observations.	Weight in Ounces.	Number of Observations.	Weight in Ounces.	Number of Observations.	Weight in Ounces.
12 ..	173	356±22	131	346±21	304	352±22
13 ..	140	371±24	105	348±22	245	361±23
14 ..	151	380±23	103	356±22	254	370±22
15 ..	190	387±23	151	363±22	341	376±22
16 ..	130	391±23	96	369±23	226	382±23
17 ..	125	408±24	100	378±24	225	395±24
18 ..	179	411±25	162	391±23	341	402±24
19 ..	116	419±24	88	396±25	204	411±24
20 ..	106	426±24	80	405±21	186	417±23
21 ..	123	431±24	101	412±25	223	424±24
22 ..	90	437±24	73	419±23	163	428±23
23 ..	68	444±25	65	426±26	133	435±25
24 ..	94	446±25	127	431±23	221	437±24

The object of this work was to obtain a smooth curve of the growth during the second year. In a previous paper the equations of the smooth curves of the first year weights were obtained. An attempt was made to fit these equations to the results in Table I, but even the addition of a fourth factor, dx^3, to the equation failed to produce a curve acceptable to all points.

Parabolas of the second degree were then fitted independently to the second-year figures and the following equations evolved:

$$\text{Males } y = 347{\cdot}786 + 10{\cdot}929x - 0{\cdot}25209x^2$$
$$\text{Females } y = 334{\cdot}954 + 7{\cdot}573x - 0{\cdot}00165x^2$$

The calculated values for y obtained by the extension of these equations are shown in Table II, whilst the smoothed curves are shown in the graph.

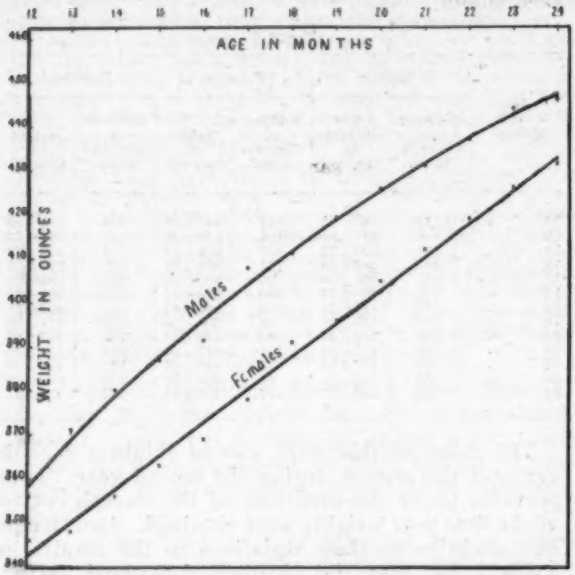
TABLE II.
Calculated Value of "y".

Age in Months.	Males.	Females.
12	358·46	342·53
13	368·64	350·10
14	378·31	357·67
15	388·47	365·24
16	396·13	372·82
17	404·28	380·39
18	411·94	387·96
19	419·06	395·44
20	425·53	402·98
21	431·87	410·52
22	437·50	418·05
23	442·63	425·58
24	447·16	433·18

It is of interest to note that whilst both equations are theoretically parabolas of the second degree, in actual practice, since the value of the x^2 factor does not reach unity, the curve obtained for the girls becomes a straight line.

Inspection of the two curves suggests that somewhere beyond the second birthday the curves for the girls would coincide with that for the boys. The

extension of the equations sets the time at about the fortieth month, a result to be doubted, as the x^2 factor of the male equation causes the curve to flatten out rapidly after the twenty-fourth month.



The two lines represent the smoothed curves of the mean weights of male and female infants. The dots and crosses are the actual mean weights obtained for each age period.

Accurate figures have not yet been obtained for the interval from the twenty-fourth to the fifty-fourth month, but the Education Department, New South Wales, has obtained a mean weight for children aged four and a half years[2] which shows that the difference between the mean weights for boys and girls is only 1·12 ounces (39·43–39·36 pounds), a difference which is not significant.

From these figures it may be assumed that somewhere about the fourth birthday the weight curves of the boys and girls coincide for a brief period, only to diverge again.

It is hoped ultimately to obtain sufficient material to produce a growth curve to bridge this interval.

Summary.

1. Weight curves for male and female Australian infants for the second year of life were obtained.

2. Observations were made upon 367 infants, of whom 172 were females and 192 males.

3. The curves obtained very closely conform to parabolas of the second degree.

4. A suggestion is offered that weight curves of male and female children coincide somewhere before the fourth birthday, only to diverge rapidly again.

Acknowledgements.

The author acknowledges his indebtedness to Dr. Sydney Morris, Director-General of Health, New South Wales, for the facilities afforded by him in the collection of data, and to Mr. J. E. Claffey, of the School of Public Health and Tropical Medicine, for his assistance in the compilation of the data.

References.

(1) F. W. Clements: "The Growth Curve of Australian Infants during the First Year of Age", THE MEDICAL JOURNAL OF AUSTRALIA, May 6, 1933, page 543.

(2) "First Report of Committee of Range of Physiological Variables in the Inhabitants of Australia and New Zealand", "The Report of the Australian and New Zealand Association for the Advancement of Science", Volume XXI, 1932, page 497.

THE REACTION OF THE DILATOR MUSCLE OF THE PUPIL TO LIGHT AND ITS BEARING ON THE ARGYLL ROBERTSON SIGN.

By KEVIN O'DAY,
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IN two papers Argyll Robertson reported five cases of "spinal disease" in which he described the characteristic features of the sign that now bears his name.[1][2] In every case "the retina was quite sensitive . . . there was marked contraction of the pupil which differed from the myosis due to other causes, in that the pupil was insensitive to light, but contracted still further during the act of accommodation for near objects, while strong solutions of atropine only induced a medium dilatation of the pupil". In two of them the pupils were of unequal size, and in the first case he observed that the pupil contracted after the instillation of the extract of Calabar bean (eserine). At the time he was interested in the pharmacology of the iris musculature and had previously published a paper on the action of the extract of Calabar bean on the eye.[3] After the publication of the first paper on "spinal disease" he performed an experiment on a rabbit to satisfy himself that atropine acted by paralysing the sphincter of the pupil.[4] It is obvious that he was a trained and careful observer.

In view of the lucidity of the original description, it is remarkable how often the term "Argyll Robertson pupil" has been misapplied, mainly through a lack of appreciation of what was quite obvious to Argyll Robertson. Both Duke-Elder[5] and Wolff[6] are content to describe it as a pupil that does not react to light whilst retaining the reaction to convergence. The term is commonly applied to dilated pupils, an error into which Continental writers, strangely enough, are not so apt to fall.[7] To Argyll Robertson the miosis was a striking feature, and, together with the poor dilatation after the instillation of atropine, was a proof that the dilator muscle of the pupil was paralysed. In an attempt to explain the phenomenon he suggests, with some diffidence, that the normal action of light on the pupil is one of "temporary reflex paralysis",[2] that the sphincter plays no active part in the light reflex, that it is a function of the dilator muscle, which relaxes when light is thrown on the eye and contracts when it is removed. If this assumption be true, paralysis of the dilator is sufficient to account for the small pupil and the loss of the light reflex.

In a recent paper, Uriarte, of Monte Video,[8] has again proposed this theory, apparently without being aware that he was drawing attention to the original explanation of Argyll Robertson.

The suggestion that dilatation of the pupil as a result of decreasing the illumination of the eye is the active part of the light reflex is one so diametrically opposed to the commonly accepted theory that it is met with frank incredulity. The final part of Argyll Robertson's paper, in which he explains his theory at some length, has been tacitly ignored. Nevertheless it accounts for many facts associated with the movements of the pupil which are difficult to explain on the assumption that the sphincter is the muscle primarily concerned with the light reflex. It is also a much more simple explanation of the Argyll Robertson sign than one which demands an interruption of the afferent pathway as well as of the sympathetic fibres supplying the dilator.[9]

The following physiological facts agree with the theory of Argyll Robertson and Uriarte.

In sleep the pupil is contracted. The deeper the sleep, the stronger is the contraction and the less it reacts to light.[10] Many ingenious attempts have been made to explain this phenomenon, which is not to be expected in the resting eye if the action of contraction to light is an active one. Under such conditions a moderately dilated pupil at least would be looked for. Once it is agreed that the dilator is alone responsible for the movements of the pupil when light falls on the eye, the contracted pupil of sleep is no longer a paradox: it is the normal condition of rest.

A pupil contracted under the influence of strong illumination will contract still further with convergence accommodation and after the instillation of eserine into the conjunctival sac, a fact noted by Argyll Robertson. Under these conditions the dilator is fully relaxed. With convergence accommodation or forcible closing of the lids the sphincter acts synergically and the pupil actively contracts. The position is similar to that occurring when the Argyll Robertson sign is present, with the exception that the dilator still retains its normal tone. The absence of this tone from the paralysed dilator explains the over-active constriction of the pupil on convergence accommodation which is such a well known feature of the Argyll Robertson sign. The constriction of eserine is merely the persistence of the synergic action of convergence accommodation which the drug allows by inhibiting the destruction of acetyl-choline.[11]

There is some embryological evidence that the dilator is actively concerned with the light reflex. Like the sphincter, it is developed from ectoderm—the outer layer of the optic vesicle. But whilst the sphincter develops fully into unstriated muscle, the dilator remains in a semi-embryonic state, only the anterior part of the cell being transformed into muscle fibre,[12] and it becomes "not a true muscle, but a contractile membrane of epithelial origin".[13] It thus bears a remarkable resemblance to the pigment epithelium of the retina of which layer, in actual fact, it is the forward continuation. Although it has never been proved in man, it is known that in lower animals the cells of the pigment epithelium of the retina send processes inwards between the outer members of the rods and cones. Under the influence of light the processes elongate inwards, and in the dark contract outwards. The muscle fibres of the dilator are nothing more than the processes of the cells of the anterior of the two posterior layers of epithelium of the iris, and their action is exactly the same as that of the processes of the retinal pigment epithelium. In the light they elongate, and in the dark they contract. The comparison may seem fanciful. It is nevertheless striking. The semi-embryonic state of development of the dilator would also explain why the pupil will contract to light after all the central connexions have been destroyed.[14] Although this primitive action is commonly attributed to the sphincter, it seems more probable that it might be retained by the more primitive dilator, the cells retaining their property of responding directly to a light stimulus.

The condition of the pupil in Horner's syndrome presents one difficulty in the way of accepting this theory. Whilst it is small, it still reacts to light. Uriarte overcomes this objection with the assumption that the paralysis is not complete. In view of the scattered course of the sympathetic fibres to the eye, his assumption is not unreasonable.

Conclusion.

In closing his second paper Argyll Robertson writes: "For a thorough solution of this question further experiments and clinical observation are necessary." Despite the enormous amount of literature that has been produced on this subject during the last seventy years, these words are just as apt a conclusion to this paper as they were to that of Argyll Robertson in 1869.

Summary.

1. Attention has been drawn to the original theory of Argyll Robertson that paralysis of the sympathetic supply to the dilator muscle of the pupil is sufficient to account for all the phenomena of the pupillary sign that bears his name.

2. Physiological facts marshalled by Uriarte in support of the theory of paralysis of the dilator have been summarized and commented on.

3. Reference to embryological facts with regard to the development of the dilator muscle of the pupil has been made to support the theories of Argyll Robertson and Uriarte.

References.

(1) D. Argyll Robertson: "On an Interesting Series of Eye Symptoms in a Case of Spinal Disease, with Remarks on the Action of Belladonna on the Iris, etc.", *The Edinburgh Medical Journal*, Volume XIV, page 696.
(2) D. Argyll Robertson: "Four Cases of Spinal Myosis, with Remarks on the Action of Light on the Pupil", *The Edinburgh Medical Journal*, Volume XV, page 486.
(3) D. Argyll Robertson: "The Calabar Bean as a New Agent in Ophthalmic Medicine", *The Edinburgh Medical Journal*, Volume VIII, page 815.
(4) D. Argyll Robertson: "Note Regarding the Action of Belladonna on the Iris", *The Edinburgh Medical Journal*, Volume XIV, page 816.

(8) William Stewart Duke-Elder: "Recent Advances in Ophthalmology", Second Edition, 1929, page 356.
(9) Eugene Wolff: "The Anatomy of the Eye and Orbit", 1933, page 213.
(10) R. Bing and A. Franceschetti: *"Kurzes Handbuch der Ophthalmologie"*, Volume VI, 1931, page 125.
(11) A. Buenefama Uriarte: *"Mouvements pupillaires: Une nouvelle théorie sur la pathogénie du signe d'Argyll Robertson"*, *Annales d'Oculistique*, Volume CLXXII, page 672.
(12) H. Houston Merritt and Merrill Moore: "The Argyll Robertson Pupil: An Anatomic-Physiologic Explanation of the Phenomenon, with a Survey of its Occurrence in Neuro-Syphilis", *Archives of Neurology and Psychiatry*, Volume XXX, page 357.
(13) R. Bing and A. Franceschetti: *Loco citato*, page 106.
(14) William Stewart Duke-Elder: *Loco citato*, Third Edition, 1934, page 121.
(15) Ida C. Mann: "The Development of the Human Eye", 1928, page 129.
(16) Speciale-Circione, quoted by R. Seefelder: *"Kurzes Handbuch der Ophthalmologie"*, Volume I, 1930, page 508.
(17) R. Bing and A. Franceschetti: *Loco citato*, page 91.

ON THE CARRIAGE OF SERUM FOR THE WASSERMANN TEST.

By CECIL J. HACKETT, M.D., M.R.C.P.,
Adelaide.

IT has been thought worth while to record the following experiences in the transport of serum over long distances. In 1934 serum collected in Darwin, Northern Territory, was carried overland to Adelaide in an initially cooled vacuum flask. The journey occupied eight days, and on arrival the specimens were found to be in satisfactory condition for examination. Venous blood was collected into sterile test tubes; the clot was separated and the serum transferred by sterile pipettes into sterile test tubes, which were sealed by heat. The syringes and needles were sterilized by boiling in hypertonic saline solution. Similarly serum was successfully carried from Ooldea, South Australia, to Adelaide. On this occasion the syringes and needles were sterilized with chloroform.

In July, 1935, fifty specimens of serum were collected from natives in the Warburton Ranges, Western Australia, carried by motor truck 350 miles to Laverton, thence by train, via Kalgoorlie, to Adelaide. The syringes and needles were sterilized by boiling in hypertonic saline solution. The serum was treated as before, except that it was finally sealed in sterile ampoules, as this was easier. Some of the specimens were then placed in a water bath at 55° C. for thirty minutes, but this did not appear to be an advantage. For transport the specimens were wrapped in a thick layer of cotton wool. On arrival in Adelaide the sera were in an entirely satisfactory condition, although some of the specimens had been collected three weeks previously.

On these occasions no high atmospheric temperatures were experienced. These facts are recorded as there are few places in Australia, where a medical man is practising, which, with modern air services, are more than a week's journey from an organized laboratory; so there are no reasons, apart from financial reasons, why serological investigation should not be used in the diagnosis of any case requiring it.

Acknowledgements.

These observations were made in the course of studies which were undertaken with the assistance of a grant from the Sheridan Research Fund of the University of Adelaide. I am also indebted to the Director of the Adelaide Hospital Laboratory and Mr. S. F. Tee for carrying out the Wassermann tests for me.

Reviews.

LARYNGOLOGY AND OTOLOGY.

"RECENT ADVANCES IN LARYNGOLOGY AND OTOLOGY", by Dr. R. Scott Stevenson, is a book to be highly recommended and the author is to be complimented on the concise way in which he has dealt with such a vast amount of material.[1] The general practitioner will find it a very easy book to read and to understand. The specialist will find the most recent advances in each special subject well described. The post-graduate worker for the D.L.O. and the F.R.C.S. diplomas will find the book of great value, and the references, which are conveniently placed at the end of each chapter, indicate the path for further study.

There are twenty-two chapters, each chapter being confined to one special subject; those under such headings as "The Tonsil Problem", "Chronic Nasal Sinusitis and its Treatment", "Ménière's Disease", "The Conservative Treatment of Chronic Middle Ear Suppuration" will be of interest to the general physician.

In the chapters dealing with the mechanism of the larynx, cancer of the larynx, theories of hearing, the mechanism of the labyrinth, and the surgical treatment of facial paralysis, the specialist will find the most recent work described. The advances in endoscopy in regard to new instruments, diagnosis and treatment are clearly indicated.

These headings will serve to give an idea of the vast amount of information to be found in this small manual.

It is difficult to pick out any one chapter for comment; they are all written very clearly with obviously a perfectly open mind. The author, however, does not hesitate to indicate the different value of different procedures. For instance, under "Chronic Nasal Sinusitis and its Treatment", the external operation of Sewell and Ferris Smith is well described, but a warning is given that all conservative procedures should be tried before such radical measures are adopted.

Amongst the various methods of treatment of tonsillar infection treatment by diathermy is considered and its limitations are indicated in such statements as: "Removal of tonsils by diathermy is not devoid of risks", and, again: "An absolutely complete removal of the tonsils is an ideal to be aimed at, but it is seldom accomplished."

The different theories regarding otosclerosis as put forward by A. A. Gray, Otto Mayer, Wittmaach and Lange, are all well described and discussed.

Altogether the reader is greatly impressed with the amount of knowledge encompassed in this small volume; he cannot fail to realize the great amount of time and labour that must have been expended in its preparation. There are 346 pages printed in clear type and the book is excellently illustrated. The publishers are to be congratulated on the excellent way in which the manual is presented.

[1] "Recent Advances in Laryngology and Otology", by R. S. Stevenson, M.D., Ch.B., F.R.C.S.; 1935. London: J. and A. Churchill. Demy 8vo, pp. 356, with illustrations. Price: 15s. net.

The Medical Journal of Australia

SATURDAY, MAY 9, 1936.

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LOUIS PASTEUR IN A TALKING FILM.

To the general public, to the film producers and to educationists cinematograph films have different values. The public seeks amusement, the film producer wants to make money, and the educationist wishes to have his message presented in film form in such a way that the public will reap benefit from what it sees and hears. The public apparently is amused, or, perhaps it would be better to say, receives the kind of entertainment that it thinks it wants. We do not believe that the majority of the public really values much of the nonsense offered to it by the film corporations. The enormous crowds that flock to see a really good film of historical or of general dramatic interest are proof of this contention. To films of the lesser breed many persons are attracted by intriguing titles, by the names of famous stars, or by boredom, because they do not know what else to do with their leisure. The film corporations undoubtedly achieve their object in making money, for they can all boast of palatial headquarters, properties and pay rolls valued at many millions, generally of dollars, not pounds. The wish of the educationist is not often gratified. His aims and aspirations have previously been discussed in these pages in connexion with the establishment of a British film institute that would be a link between producer and consumer and that would interpret to the trade the needs of a great variety of organizations wishing to use non-theatrical films. (See THE MEDICAL JOURNAL OF AUSTRALIA, December 22, 1934, page 817.) According to recent reports, this institute has already done useful work. When a film of real value has been produced, the educationist should see that the greatest possible use is made of it.

Warner Brothers, First National Pictures Limited, have prepared a talking film entitled "The Story of Louis Pasteur", which will shortly be shown in Australia. This film, in spite of certain distortions, is, for preventive medicine, propaganda of the highest order. Pasteur's struggle to establish the truth of his germ theory of disease is depicted with dramatic force. In puerperal fever he is shown as basing his work on the observations of Semmelweis, and he insists that infection is conveyed from one puerperal woman to another by the medical attendant and midwife. His work on anthrax and its value to France at the time of the Franco-Prussian War are well illustrated; the most is made of the test inoculation with anthrax of some sheep, half of which had and half of which had not been submitted to his "vaccination". Joseph Meister, the Alsatian boy, is brought to Pasteur after having been bitten two days previously by a mad dog. Pasteur is not yet ready to treat human beings, but he courageously gives the boy the treatment that he has used for his laboratory animals, and the boy recovers. Finally, at the Sorbonne Pasteur is received by a vast concourse of people and Lister embraces him. In the film he makes his reply, calling on those of the younger generation to follow the call of science to unravel the mysteries of Nature. Actually this speech, on account of Pasteur's weakness, was made by his son. Some distortions have been mentioned. It is a pity that film producers should always deem it necessary to make their own story out of any chain of events; in other words, that they should try to improve on history. Mr. Creswell O'Reilly, the Chief Commonwealth Film Censor, according to the newspapers, stated in his recent report that probably no transcription of a play, book or event to the medium of the screen would ever be accom-

plished without modification of the material used. He is reported to have added that the film had outdistanced all its predecessors as a tamperer with the truth. These are hard words, but if they are in the least measure effective in preventing distortion of facts they will have been spoken to some purpose. In the present instance the sequence of events has been considerably altered and incidents have been added, presumably to make a more dramatic tale. Pasteur wishes the villain of the piece, a noted obstetrician and his arch enemy, to attend his daughter in confinement when no other attendant is available. The obstetrician makes Pasteur sign a declaration that his investigations of the causes of hydrophobia have proved fruitless and of no value—this is the price of the obstetrician's attendance. Certain conditions surround the signing of the paper. The incident is, of course, fictitious; to manufacture it is surely unjust to the memory of a great man and unjust to those who opposed his views, short-sighted and pig-headed though they were.

In spite of the historical inaccuracies of this film, we would urge medical practitioners to see it as soon as it is released and to talk about it amongst their patients. It will give the uninitiated some idea of the darkness that reigned before Pasteur did his great work, and of the blessings that have come to humanity since. Although it is really outside the scope of the present discussion, we would draw attention to the superb acting of Paul Muni, who takes the part of Pasteur and who has been made up to look extraordinarily like his pictures. Warner Brothers are to be congratulated on having undertaken this work; the medical profession will wish the film success.

Current Comment.

THE USE OF HYPERTONIC SALINE SOLUTION IN CORONARY ARTERY DISEASE.

FOLLOWING the work of Silbert and others, favourable results have been obtained in *thromboangiitis obliterans* by the use of intravenous injections of hypertonic saline solutions. Not all observers have been equally enthusiastic, however, and some have thought that the good results have been equally due to the prolonged care and other treatment given the patients. A new and interesting light is shed on the subject by an article by S. C. Feinberg, who has used injections of hypertonic saline solution in the treatment of coronary artery disease.[1] Feinberg felt for some years that such a line of treatment was logical, but hesitated to follow it until a few years ago, when he treated a patient for arteriosclerotic closure of the vessels of the leg in this way, and later discovered that this patient also suffered from coronary artery disease. Not only was the procedure well tolerated, but the patient was relieved of the attacks of effort angina from which he had previously suffered, and accordingly treatment was continued. A 5% sodium chloride solution was used in a dose of 300 cubic centimetres; it was injected into a vein three times a week. It is surprising to learn that this patient was treated continuously for three years and is still receiving a weekly injection. During this three-year period similar treatment has been given to fifteen other patients suffering from combined distal and cardiac arteriosclerotic occlusion. In addition, six patients with *angina pectoris* due to coronary disease, five of whom had had occlusion of a coronary vessel, have received the same treatment, and all have benefited to a striking extent after the failure of the usual routine measures. The actual method now employed by the author is to inject an initial dose of 100 cubic centimetres of 5% saline solution; this is repeated three times a week, the dose being increased by 50 cubic centimetres weekly till a maximum of 250 is reached. If precordial pain is complained of during or immediately after an injection, the dose is reduced temporarily and then cautiously increased. The solution was introduced by gravity from a burette about three and a half feet above the patient. The patients were allowed to come to the clinic as out-patients, and it was not considered necessary that they should be accompanied by a relative or friend. While they were receiving the treatment no other drugs were used.

Feinberg, in discussing his results, remarks that perhaps it will be contended that the improvement in his patients was of psychogenic origin, since these patients are usually "heart conscious". He believes, however, that the improvement was too striking and too well maintained to be explained thus, and points out that the patients selected were those who had failed to respond to the usual procedures. Feinberg does not claim that the underlying arteriosclerotic process is arrested, but that the collateral circulation is improved in the heart. The contraindications he gives are nephritis, failure of cardiac compensation, the more serious forms of arrhythmia, and hypertension.

SCARLET FEVER.

THE streptococcus, particularly of the hæmolytic type, is now known to be a causative factor in a very wide range of ailments, a range wider far than

[1] *The American Journal of the Medical Sciences*, March, 1936.

was imagined a few years ago. Much research yet remains to be done before the damage of which various strains of this organism are capable has been determined. But from the clinical point of view it is urgently necessary that some more scientific classification of streptococcal diseases should be adopted than any now in use. What is scarlet fever for instance? Is it a separate disease, a clinical entity, or merely the manifestation in certain patients of their reactions to invasion by a certain type of streptococcus? May not a patient attacked by the same organism be as gravely ill, even though he have no characteristic rash or sore throat, as the patient with the typical angina and punctate erythema of scarlet fever, so-called? Is it safe to allow the former patient to remain at large while the latter is isolated in an "infectious" ward? In short, is the term "scarlet fever" and the practice of notification and segregation now applied to persons adjudged to be suffering from it of any social or therapeutic value?

These pertinent queries are propounded in an admirable paper recently written by F. G. Hobson[1] and have greatly stimulated the interest of workers in epidemiology. These latter agree for the most part with Hobson's statements, but find extreme difficulty in suggesting any workable substitute for the present system of control. The very diagnosis of scarlet fever has in the past very often baffled clinicians. This fact was explained on the hypothesis that the severity of the signs and symptoms of the disease varied with different epidemics, according to the virulence of the infecting organism. In the nineties there was a good deal of head-scratching over the diagnosis. Amid the confusion Clement Dukes asked his colleagues: "Is it possible that there is a Fourth Disease?" Apparently there was—a queer mixture of scarlatina with resemblances to measles and touches of *rötheln*. This strange child ("with its father's eyes, but its mother's nose and mouth", as a wag of the day described it) was scarce born before it was followed by two brothers, the fifth and sixth diseases, sometimes respectively called *erythema infectiosum* and *exanthema subitum*.

Whatever may have been the causal organisms concerned in the appearance of these alleged diseases, it now seems evident that there is no one special germ responsible for the clinical picture called scarlet fever, although numerous strains of streptococci, especially the toxigenic hæmolytic strains, give rise to exotoxins possessing erythrogenic powers.

Thirteen years ago the Dicks were able to produce clinical scarlet fever by using a strain of hæmolytic stroptococcus isolated by themselves, and to prove that after such an attack a "Dick-positive" person became "Dick-negative" (horrible phrase). All this seemed to throw light on the problems of the origin and infectivity of the disease, until research led to the discovery of a further thirty strains of streptococci—all hæmolytic, but by no means always related to the appearance of erythema. More confusing still was the certainty that some non-hæmolytic streptococci were found to be present in cases of typical erythema and in patients who exhibited all the clinical features and suffered from all the sequelæ of scarlet fever.

In Hobson's opinion, then, the streptococci which are pathogenic to man have a consequential connexion with a large number of pathological conditions closely related one to the other. These pathological states, due to the passage of the organisms along the blood or lymph streams, may be associated with erythema or not, no matter whether a non-hæmolytic or a hæmolytic streptococcus is concerned. As an illustration of these points the case is cited of a hospital superintendent who infected an abraded finger while dressing a suppurating gland on the neck of a patient suffering from scarlet fever. The doctor died within a few days of streptococcal septicæmia, but throughout the illness there was never any erythema. A further interesting history is that of a woman who during her puerperium developed an erythematous rash after the repair of a small perineal tear. From the wound itself hæmolytic streptococci were recovered. The patient's fauces yielded a culture of non-hæmolytic organisms and a hæmolytic strain was grown in a blood culture. Cases are also recorded of acute tonsillitis (in one instance followed by death) due to streptococci of both varieties in which the presence or absence of the rash was inconstant.

The deduction which Hobson draws from these and other similar facts is that erythema is a variable feature in infections caused by hæmolytic streptococci, and by no means rare in those due to non-hæmolytic strains. And although the rash is perhaps commoner in diseases due to *Streptococcus hæmolyticus*, it is a poor means of estimating the course and prognosis in any one patient. Further, an infection associated with a non-hæmolytic streptococcus may be followed by sequelæ indistinguishable from those due to a hæmolytic strain, whether an erythema be present or not. It follows that the criteria (rash, erythema) which now determine the notification of cases of scarlet fever and the isolation of the sufferer are of little use as weapons in the control of epidemics. Such methods do nothing more than restrict the services of specialized hospitals to an arbitrarily selected group of patients. As these patients are not all suffering, necessarily, from the same illness, the regulations governing their isolation should be made more rigid than at present, if such rules are to possess any practical value. It may be that a wider use of the swab stick for the identification of various types of streptococci, as well as of diphtheria bacilli, might help to disabuse the public mind of the common belief that tonsillitis is a trivial disease. No less than the control of diphtheria, that of streptococcal infections is of pressing public importance. These infections and their sequelæ are one of the major problems of medicine, if only from their economic consequences.

[1] *The Lancet*, February 22, 1936.

Abstracts from Current Medical Literature.

OPHTHALMOLOGY.

Late Traumatic Rosette Cataract.

L. LUGLI (*Archives of Ophthalmology*, September, 1935) describes, with illustrations, six cases of rosette cataract. The literature is very recent, beginning with Vogt in 1922; the latest work is a study on contusion cataracts published by Cattaneo in 1934. This type of cataract is of traumatic origin, sometimes associated with dislocation of the lens and dialysis of the iris. The opacity in the lens assumes various forms—pulverulent, woolly, resembling single or fused rose petals, feather-shaped. The opacities originate from the sutural system of the anterior cortex, assuming the form of many rays and a radial direction. The age of the cataract may be ascertained from the distance between the anterior disjunction band and the plane of the rosette opacity. The rosette cataract may be considered as stationary.

Ocular Disorders Associated with the Wisdom Tooth.

C. B. HENRY (*British Journal of Ophthalmology*, July, 1935) is convinced that a perfectly healthy but unerupted wisdom tooth may produce disturbances in the eyes owing to pressure on neighbouring nerves or to reflex irritation. Of 700 cases he has studied, 50 were associated with some ocular symptoms. Radiographic examination should always include those areas where wisdom teeth may be buried. A man of forty-two had recurrent iritis. After the second attack an impacted left upper third molar was discovered by X rays. He refused extraction and after seven months had a third attack. Extraction effected a cure. A woman of twenty-two had periodic twitching and pulling of the right eyelid for three and a half years, with headache and face-ache. At length a right wisdom tooth was extracted with relief of symptoms. Other cases were associated with paresis of muscles.

Electrosurgical Extirpation of Xanthoma of the Eyelids.

ACCORDING to L. J. Gorman Silvers (*The Journal of the American Medical Association*, September 7, 1935), *xanthoma palpebrarum* is a fatty degeneration of the orbicularis. The cutis is packed with cell-like masses known as xanthoma cells, which are the degenerated remains of muscle fibres and sarcolemma nuclei. After infiltration anæsthesia a small pointed needle electrode connected to the Oudin or monoterminal high frequency outlet is employed. A current strength that will produce a millimetre spark on fulguration is essential. The fatty fibres are desiccated by the penetrating active electrode. The biterminal or coagulating current must be avoided, as it produces scarring. Treatment is given to ambulant patients every week.

Coley's Mixed Toxins in Ophthalmology.

J. LEVINE (*Archives of Ophthalmology*, October, 1935) again reports upon the advantages of Coley's mixed toxins as a foreign protein. It is a vaccine made from killed cultures of *Streptococcus erysipelatus* and *Bacillus prodigiosus*. It is a concentrated red-coloured fluid put up in rubber-capped glass vials; it keeps well in an ice-box and preserves its efficiency for years. It is injected into the deltoid muscle in an average dose of three minims. Less may be given to children, and seldom as much and never more than six minims. Invariably the reaction occurs in six hours and the temperature varies between 38·3° and 39·4° C. (101° and 103° F.), lasting from three to four hours. It may be given every third day as often as necessary. It is used in any condition suitable for protein therapy, including secondary glaucoma and sympathetic ophthalmitis. The results are often astounding. Its cheapness and ease of administration are among many advantages over other agents.

Sympathetic Ophthalmia.

IN response to a *questionnaire* in New York State, 82 physicians reported 158 cases of sympathetic disease. Only 48 of the 126 enucleated eyes were examined microscopically, and the diagnosis was confirmed in 41 cases. From these data, H. H. Joy (*Archives of Ophthalmology*, November, 1935) presents a report. The disease is not decreasing in frequency. In 63·5% it followed a perforating wound; in 19·5% it followed an intraocular operation; in five of these cases (12·2%) the operation was cataract extraction. Other causes were non-perforating injury, perforating corneal ulcer, *phthisis bulbi* following measles, and necrotic sarcoma of the chorioid. In only one patient did the onset occur less than three weeks after the injury. In 16 patients the period was from three weeks to two months, and in 12 from three months to one year. Larger intervals are reported: 6, 17, 11, 20, 24 years. The prophylactic value of enucleation is greatest immediately after the injury and it diminishes markedly with lapse of time. Dor maintains that if enucleation is delayed as long as two weeks its effect is invariably lost, and the author thinks that his series seems to confirm Dor's contention. Six eyes were removed before the onset of sympathetic disease in the other eye, yet infection followed, severely in five cases and mildly in one. In the one mild case the exciting eye was removed two weeks after the injury. The interval between enucleation and involvement of the remaining eye ranged between two days and two months. The disease in children is severe and the outcome unfavourable.

Ophthalmomyiasis.

W. B. ANDERSON (*American Journal of Ophthalmology*, August, 1935) reports a case of *ophthalmomyiasis interna*; only eighteen cases have been reported. A man of forty-six felt a light blow in the left eye, followed by some discomfort and soon afterwards by the presence of a crescentic object in the field. This soon disappeared, but the patient suffered intense paroxysms of pain. The iris became slightly turbid, also the media. On the seventh day the pain ceased suddenly and the object in the visual field returned. It could be easily seen with the ophthalmoscope and identified as a larva—possibly of the *Gastrophilus intestinalis*. No surgical interference was advised. The larva died and the patient retained his sight.

Subjective Lightning Streaks.

R. FOSTER MOORE (*British Journal of Ophthalmology*, October, 1935) has collected twenty-six cases of subjective lightning streaks, mostly in women over forty years of age. A typical history reads thus: "Flashes of light just like lightning to the outer side of the right eye . . . . First saw them in the daylight and now chiefly come on at 5.30 p.m. Seen every day for the last three months." Most of the patients complain of spots following the lights. The author has followed these patients sufficiently long to be sure that the symptoms are not the precursors of any serious fundus disease. The cause is doubtful; the condition is possibly due to the rupture of a peripheral retinal cyst.

OTO-RHINO-LARYNGOLOGY.

Contact Ulcer of the Larynx.

CHEVALIER JACKSON AND CHEVALIER L. JACKSON (*Archives of Otolaryngology*, July, 1935) describe contact ulcer of the larynx as a disease characterized by distinctive location, ætiology, pathological process and course and an interminable duration unless it is recognized and properly treated. It is usually overlooked; when seen, it is usually mistaken for cancer or tuberculosis. The exciting cause is vocal abuse. The perpetuating cause is necrosis of the tip of the vocal process of the arytenoid cartilage located in the bed of the ulcer. The diagnosis is made by mirror examination, by direct laryngoscopy and, rarely, by biopsy. The regimen of silence is the most important part of treatment. If the talkative patient cannot be controlled, he will frustrate

all efforts to cure the condition. Excision of accompanying granuloma is sometimes necessary, and in some instances the ulcer itself may require excision. These measures, however, must be carried out with extreme neatness and delicacy, or irreparable damage may be done. Silver nitrate and other similar local applications are worse than useless.

Treatment of Thrombosis of the Lateral Sinus.

PHILIP E. MELTZER (*Archives of Otolaryngology*, August, 1935) gives a summary of the results of treatment of thrombosis of the lateral sinus obtained during twelve years at the Massachusetts Eye and Ear Infirmary. Symptomatically it is impossible to distinguish between sinus thrombosis and phlebitis. In a total of 4,961 cases of resection of the mastoid the diagnosis of sinus thrombosis was made in 161 instances, indicating that it occurred once in approximately 31 cases. Sinus thrombosis is the most frequent complication of mastoiditis, the greater number of cases occurring in association with acute otitis. It occurred more often in patients between eleven and twenty years of age, the curve of incidence tapering off sharply at both extremities of age. Metastasis was an uncommon complication before ligation of the jugular vein. Involvement of the joints was the most common complication, the greatest number of cases occurring after ligation and treatment of the sinus. Involvement of the joints adds to the seriousness of the disease, as it may prove to be the focus which continues to feed organisms into the blood stream. Blood cultures are of value as an aid in establishing a diagnosis or at least in focusing attention on the lateral sinus. In the presence of continuing symptoms negative results of blood culture should not contraindicate examination of the sinus. The Ayer-Tobey test is a valuable diagnostic aid. The reliability of the test is dependent on the experience and carefulness of the person making the test. The records bear out definitely the common knowledge that the appearance of the sinus gives no indication of what may be within it. There is more reason, however, to suspect injury to the endothelial lining in cases in which there is a perisinuous abscess. Sinus thrombosis is not necessarily fatal if not treated surgically. In the author's opinion, operation is always indicated as the best means of aiding the patient to overcome the infection, affording drainage, which thereby tends to limit the disease. Extirpation of the focus of disease is an impossibility; the surgeon merely aids the patient. The battle for supremacy is between the infecting organism and the patient's power of resistance. Post-operative sinus thrombosis occurs infrequently as compared with the manifest and latent types of thrombosis. Secondary infection of the wound of the neck occurs fairly commonly. The percentage of fatalities in general may be considered to be between 20% and 30%. In this report the patients who were hopelessly ill on admission were excluded. In the combined series there were 148 patients, of whom 32, or 21·7%, died and 116, or 78·3%, recovered. Excluding intracranial disease, sinus thrombosis must be considered to have a relatively high mortality rate.

Facial Paralysis.

OLIVER P. BOURBON (*Archives of Otolaryngology*, September, 1935) discusses facial paralysis and its treatment and includes a description of the technique of galvanic treatment. An examination of the ears should be made by an otologist in every case. While in some cases of mild degree recovery is spontaneous and in others recovery occurs in a reasonably short time with rest and proper treatment, the majority of cases require intelligent, energetic and long-continued care and treatment to bring about recovery, which even then may not include a complete return of function. Satisfactory results are usually obtained, except when the condition is caused by neoplastic infiltration, or when there is a complete break in the continuity of the nerve, whether the break is caused by unrelieved pressure, necrosis of the mastoid, operative accident or accidental injury. Even if the paralysis has lasted for a year or longer, treatment should be given faithfully and energetically, because partial recovery is sometimes obtained. A loss of electrical reaction should not cause discouragement unless it is complete or nearly complete, because functional recovery always precedes recovery of electrical reaction. Ney has expressed the belief that after injury and surgical intervention, even though the nerve is completely severed within the temporal bone, its firm attachment to the periosteum of the facial canal does not permit its ends to retract; that the ends should maintain sufficient approximation to permit the regeneration of the nerve fibres of the proximal segment to reach those of the distal segment; and that failure to regenerate is probably due to the presence of fragments of bone. When a nerve has been completely divided the sixth month should show the first evidence of returning voluntary power. When no improvement has occurred after six months of treatment, prognosis is poor, and after more than one year further treatment is useless and the problem goes into the realm of neurosurgery.

Œsophageal Affections in Young Children.

BROWN KELLY (*The Journal of Laryngology and Otology*, February, 1936) describes some cases of œsophageal disease in young children and concludes that shortening of the œsophagus may be congenital or postnatal, or may begin before birth and continue to develop after birth. Congenital shortening of the œsophagus and the associated thoracic stomach are not so rare as at first supposed. In the early years of life the cardiac canal is liable to spasmodic closure, which causes regurgitation and wasting; the closure can be overcome by passing a bougie, and operation is not needed. In later childhood there is less trouble from spasm. The author knows of no death which could be directly attributed to inanition caused by obstruction of the cardiac canal of a congenitally short œsophagus. Necropsies on adults have proved that the presence of a thoracic stomach due to congenital shortening of the œsophagus does not preclude the attainment of healthy old age. Post-natal shortening and narrowing of the œsophagus were found in two cases owing to spasm and associated with a large hiatal hernia. A spasm of the cardiac canal and at the lower end of the thoracic œsophagus gave a characteristic radiological appearance, as shown in two cases. In several of the cases described the shortening of the œsophagus was evidently due to both ante-natal and post-natal factors. The latter were mainly of the nature of an ascending fibrosis. This condition proved fatal in several instances.

Effect of Physical Agents on the Temperature of the Nasal Sinuses.

HARRY K. TEBBUTT (*Archives of Otolaryngology*, December, 1935) discusses the effect of physical agents on the temperature of the nasal sinuses, and gives his experimental observations. Cold compresses, an icebag, hot compresses, a hot water bottle, an electric heating pad and a lamp for the radiation of infra-red rays were used to apply heat to the face in the region over the sinuses, and the whole head was heated in the field of a high frequency oscillating current of from 9,000 to 12,000 kilocycles. Readings of the changes of temperature within the maxillary and sphenoidal sinuses were made. No changes in the temperature were noted when ice compresses, an ice-bag, a hot water bottle, an electric heating pad or hot compresses were used. A drop of about 1° F. in the temperature of these sinuses occurred when the infra-red rays and the high frequency oscillating current were used. This drop was unexpected, but it was accounted for by the evaporation of the increased nasal secretions which accompanied the use of these agents. The author is of the opinion that the oscillator and the lamp are two agents of great value in the treatment of acute and subacute infections of the sinuses, for it has been shown that there is a definite increase of thin serous discharge from the nose and sinuses when they are used. This obviously improves the drainage and hastens resolution.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Queensland Branch of the British Medical Association was held at the Hospital for Sick Children, Brisbane, on February 7, 1936. The meeting took the form of a series of demonstrations by members of the honorary medical staff. Part of this report appeared in the issue of May 2, 1936.

Osteomyelitis of the Skull.

DR. J. G. AVERY showed a boy suffering from osteomyelitis of the skull, which was a comparatively rare condition and comprised only 1% to 2% of all cases of acute osteomyelitis.

The boy was first seen in the medical department of the Hospital for Sick Children in September, 1934, and again in July, 1935, with recurrent abdominal pains and vomiting. No sign of lead poisoning was found; the boy was not a nail-biter. He did not suffer from diarrhœa and his Wassermann test gave no reaction. He was referred to Dr. Avery with regard to the surgical condition of his abdomen, but Dr. Avery could find no reason for interference. In October, 1935, the boy complained of a tender swelling over the left side of the scalp; an abscess was opened, pus was evacuated and the boy was treated as an out-patient till later in October when he was sent to the convalescent home at Sandgate. He returned to hospital in November, 1935, with a fluctuating swelling in the scalp, higher up over the parietal bone. An X ray examination revealed very slight erosion of bone. Another X ray examination in January, 1935, revealed sequestra. An operation was performed and two sequestra were removed from one wound, and one, comprising the whole thickness of the skull bone, from another. The posterior wound had healed rapidly. Dr. Avery questioned whether a more extensive operation, with drilling of the skull and letting the pus out, might have saved the shedding of bone. The X ray picture showed that a considerable area of parietal bone was involved. There was no history of injury to the head, of furunculosis or any skin condition or mastoid condition. The abdominal condition had not given any further trouble.

Undescended Testicle: Non-Operative Treatment.

DR. L. G. HILL discussed the question of the treatment of the undescended testicle with hormonic methods, giving the substance intramuscularly, as an alternative to operative treatment. The work done on the presence of hormones in the urine in connexion with the Aschheim-Zondek experiments had been carried further, and it was found that injections of hormone substance produced definite changes in the testis of the rabbit. Spence, over a year ago in London, had shown a series of cases in which he had used "Pregnol". The Americans were using "Antuitrin S".

Dr. Hill had tried a small series with "Antuitrin S". He showed a boy whose left testis had been completely undescended; it was now in the scrotum. The boy had had 2,000 units by injections. Considerable divergence of opinion as to the dosage was evident; the Americans were using very much smaller doses than some of the English workers. In some cases doses were given varying from 3,000 to 16,000 units; in other early cases 200 units were given daily for two or three weeks and then the time of the injections was spread out. The Americans more often gave 100 units thrice a week or 200 units twice a week. Dr. Hill had been giving 500 units once a week.

He showed another boy whose testis had not previously been felt, but had now come to the external ring; it could not be pushed further and had a slight hernia above it; this boy had had 3,500 units. The risk of hernia had to be considered, also the possibility of general changes in the testis. Experimental work had shown that this would not be very great; any progress in the testis was reversed later. Changes in the external genitals took place and tended to remain permanent. The unilateral undescended testis reacted very much better to this treatment than the bilateral testis. The testis increased in size, even when it did not come down. A patient operated on not entirely successfully had been given three small injections after operation, with definite increase in the size of the testis. The question arose: would these testes, if left alone, descend into the scrotum? Many left alone descended at puberty. The rapidity with which the testis did descend after the injections Dr. Hill considered was proof that the injections did good. The tissues and ligaments softened and allowed the testis to come down. He thought that all patients should be given the chance of this treatment before operation. "Antuitrin S" and other injection treatment would not do any good if definite adhesions were present.

Undescended Testicle: Operative Treatment.

DR. K. B. FRASER said that there was no doubt that the exhibition of "Antuitrin S" and similar substances was a great advance in the treatment of undescended testes; it was difficult, however, to estimate at the present stage to what extent surgical treatment would be rendered unnecessary. In assessing the true value of "Antuitrin S" it should not be forgotten that a certain number of undescended testes did continue to descend spontaneously up to at least the age of four years, and, according to some observers, including McCutcheon, of Melbourne, even up to the age of puberty. Further, in those instances in which there was a strong and active cremasteric reflex, the testis was at times drawn right out of the scrotum and might be seen to disappear into the canal. These, however, were not true undescended testes and were to be rigidly excluded from any series in which the potency of subcutaneous injections was being investigated.

It was well known that the descent of the testicle during intrauterine life was controlled by the *gubernaculum testis*, which had a wide lower attachment to the *symphysis pubis*, the scrotum and the groin. In many cases in which descent had been arrested the faulty attachment of the *gubernaculum testis* could actually be demonstrated at operation. It seemed, therefore, logical to assume that any case in which there was gross anatomical abnormality of the gubernacular attachment would not be influenced by any injection of gland extracts. Samuel Cohn, who had written extensively in *The Journal of the American Medical Association* on this question, summed up the position very well. He stated:

> The anterior pituitary-like principle of pregnancy urine is apparently effective in causing descent of the testicle when there is no anatomic malformation acting as a mechanical obstruction; when obstruction exists a partial descent will occur, but operation will be required to complete the process. In surgical cases the anterior pituitary-like principle is a valuable adjunct in the production of a successful outcome.

With the object of obtaining some definite data regarding the results of surgical interference in these cases, Dr. Fraser had made an attempt to get into touch with those children operated on at the Hospital for Sick Children, Brisbane, during recent years. This presented difficulty, but he was able to locate twenty patients and obtained some interesting information. Twelve cases were right-sided and eight left-sided. In regard to twelve of the twenty patients, two years or more had elapsed between the time of the operation and the reexamination, and five of them had reached adult life. The age at operation varied from one year to eleven years. Of the twenty patients operated on, eight showed a normally developed testis in normal position. In four cases the testis was slightly higher in the scrotum and slightly smaller than the testis on the opposite side, but was obviously developing normally. Therefore twelve out of the twenty cases, or 60%, showed an excellent result. Of the remaining eight patients, five had the testis in the scrotum, but it was more or less atrophied, and probably of doubtful

functional usefulness. One had an atrophied testis at the upper limit of the scrotum; one a normal testis still lying in its original position at the external inguinal ring. In the final case the history was that the testis had retracted to the external inguinal ring one week after operation, but when the boy was examined eleven years later no sign of it could be seen or felt. An associated hernia was present in almost every instance. No recurrent hernia or keloid scarring was noticed, and none of the patients complained of any post-operative pain or discomfort.

The influence of age on the success of the operation was noticeable. There was only one success out of four operations in the first four years of life; from the fifth to the eighth year, inclusive, there were five successes out of eight, and from the ninth to the twelfth year, inclusive, there were six successes out of eight. At least ten of the operation records in this series showed that the testicle seemed definitely rudimentary in type. In assessing these results any doubtful cases were considered as provisional failures, though three or four were being reexamined periodically and had not yet reached an age when further development could not reasonably be expected. Reliable statistics on the post-operative results of orchidopexy were somewhat scanty. In 1908 Rawlings investigated the results of forty cases. He had reported them in *The Practitioner* as follows: Moderately good results were obtained in four cases; three cases "promised favourably"; eight patients were not traced; and twenty-five cases were classed as failures. Much better results had been obtained in a series of eighty-three undescended testes observed in young army recruits in Stockholm in 1934; sixty-eight operations were performed. The results were excellent in forty-seven, good in sixteen, and less good in five. No definition of "good" and "less good" had been given in this series, and, as only fifteen ex-patients presented themselves for reexamination and the remaining figures were obtained from answers to a *questionnaire*, the results should be taken with considerable caution.

Taking the results of the series of twenty cases from the Hospital for Sick Children as a rough guide to the relative success of surgery, certain important factors should be considered in coming to a decision as to whether operation was indicated for this condition. First, injection treatment should, of course, be given a reasonable chance, but as yet there was no guide as to what period should elapse beyond which no result might reasonably be expected; further, from knowledge of results observed in animal experimentation, it should be established that no untoward effects were possible in regard to subsequent internal and external secretory activity following this treatment. Secondly, associated hernia was almost always present in Dr. Fraser's experience, and, when the testis lay just below the external inguinal ring, it was particularly liable to attacks of strangulation; torsion of the cord with considerable pain and subacute orchitis was also noticed. Thirdly, it was a well accepted fact that testes which remained in the inguinal canal or just below it underwent degeneration and progressive atrophy and were not capable of spermatogenesis until they were placed in the scrotum. This progressive atrophy in undescended testes was, according to some authorities, due to the greater heat experienced and the absence of a heat-regulating mechanism such as existed in the scrotum. An interesting analysis of twenty-four museum specimens of retained testes removed from adults was recently made by Pace, of the Section of Urology at the Mayo Clinic. Careful microscopical examination of longitudinal and horizontal sections led to the conclusion that regeneration of tubules and secretory activity might conceivably occur in testes replaced in the scrotum before the age of forty. Fourthly, undescended testes lying in the inguinal canal or between the external inguinal ring and the pubes had a definite tendency to sarcomatous degeneration; this was probably in part due to exposure to repeated trauma from muscle action and external injury. Three of the museum specimens previously mentioned showed signs of malignant degeneration on section.

Taking all these facts into consideration, and from experience at the Hospital for Sick Children, certain more or less definite rules could be laid down. (i) No operation should be performed before four years of age, except in special circumstances. (ii) Intraabdominal testes, if unilateral, should be left alone, as they were not subject to any special risk of sarcomatous degeneration; if bilateral, they should be left alone, unless stunting of growth and failure of sexual development were evident. (iii) Operation for testis lying in the inguinal canal or at the external inguinal ring should be performed about the sixth year. (iv) Undescended testes lying lower than the external inguinal ring should not be operated on before puberty unless subjected to repeated injury, as they belonged to the group in which there was only minor abnormality of the *gubernaculum testis*, and they might possibly descend spontaneously.

Dr. Fraser went on to discuss the operation. He said that the septal operation (Ombrédanne's method) had been performed in the majority of cases at the Hospital for Sick Children. Adequate mobilization of the cord by freeing it from the fascial sheaths and division of the gubernacular attachments were vital to success. Professor Fraser stated that the veins of the pampiniform plexus might be divided, but they should be retained if possible. The testis was placed in the scrotal sac of the opposite side through a small opening in the scrotal septum, and no anchoring sutures were necessary. Dr. Fraser thought that the whole success of the operation depended on placing the testis adequately in the scrotum without tension, and preferably without cutting any of the veins of the cord. He could not see that the Torek or any other method had any advantage over that operation in which retraction of the testis was gently inhibited over an indefinite period by the elastic action of the septum and the weight of the scrotum and normal testis, rather than by any more unyielding retentive measures.

Dr. Fraser then presented four patients of the series to illustrate the results of surgical treatment; three of them showed completely successful results; the fourth was classed as a failure, but the size of the apparently atrophied testis had increased in the last year. The last case was a suitable one in which to try the effect of "Antuitrin S" as an adjunct to surgical treatment.

Thrombocytopenic Purpura.

DR. S. F. MCDONALD showed for DR. T. R. BIGGS a child who had been in perfect health till two months previously, when he had begun to bruise very easily. He had had a fall and was admitted to hospital with two black eyes. A tourniquet was put round the arm to take the systolic blood pressure, and bleeding had developed round the area. The diagnosis was definitely that of purpura. A blood count taken on January 29, 1936, had revealed 3,610,000 red cells per cubic millimetre, 8,800 white cells per cubic millimetre, of which neutrophile cells comprised 63%, lymphocytes 36%, and eosinophile cells 1%. The hæmoglobin value was 76%. The platelet count was 15,600, normal being 800,000. Bleeding time was four minutes; coagulation time was two and a half to three and a half minutes. There was no history of abdominal pain or of gastric upset; there was bruising round the eyes; the urine was clear. On February 3, 1936, the red cells numbered 4,000,000 per cubic millimetre and the hæmoglobin value was 78%. Platelets had risen to 30,000. The bleeding and coagulation times were the same, and the fragility test gave a normal result. On February 7, 1936, the platelets had fallen again to 13,000. It was suggested that the patient be referred to a surgeon. These patients should always be given a transfusion before operation for splenectomy. The spleen was not usually found enlarged. No operation should be performed while the patient was in the acute stage of the disease, but in the chronic stage patients did very well.

Three Cases of Paralysis.

Dr. McDonald showed a boy, aged seven years, who had been in the Hospital for Sick Children for fourteen

days. Three or four days before admission he had complained of being tired and off colour. He went to bed not feeling very well and in the morning woke complaining of inability to use his arms or legs. He was admitted to hospital with a complete flaccid paralysis. Examination of the cerebro-spinal fluid had revealed no abnormality. The boy had no fever; he had vomited a little. He was probably suffering from acute infantile paralysis with no prodromal stage. Dr. McDonald said that he had seen several such cases during the year; the chance of giving serum to these patients was gone. This boy had had deltoid splints and pelvic plasters applied.

Dr. McDonald's next patient was a boy who was admitted to hospital three months previously. He had given a history of having had a convulsion that morning and another in the afternoon, and was practically unconscious on admission to hospital. He recovered and it was found that the right side of the body showed a complete spastic paralysis. At the time of the meeting there was still weakness of the right side of the face and of the speech muscles, but these were improving. The child could write well. All tests for a cerebral tumour failed to reveal one. If there had been a hæmorrhage, it had been confined to a small area, as the child's condition was improving so much.

Dr. McDonald also showed a boy who a year previously noticed that he was not able to raise his arm from his side when he was walking. In April, 1935, it was noticed that he was dragging his toe. In June, 1935, he lost the power in his right arm, then the power in the right side of his face. The paralysis affected the right side, but he could speak, as he was left-handed. The night before the meeting he had had a left-sided fit, which had upset the picture of a right-sided spastic paralysis. The abdominal reflexes were absent; before the left-sided convulsion the right had been weaker than the left. A lumbar puncture was performed, but the cerebro-spinal fluid was not under increased pressure. "Luminal" was given intravenously. The Wassermann test applied to the blood and cerebro-spinal fluid gave no reaction. Papilloedema was present. The diagnosis seemed to rest between a new-growth, disseminated sclerosis, for which the boy was very young, and Kinnear Wilson's disease, which generally showed more tremor and emotion.

Tuberculous Disease of the Hip.

DR. J. G. WAGNER showed a boy, aged five years, who complained of a limp for a period of two years, and a lump in the region of the left thigh for six months. The onset of the limp had been gradual, the child coming home and saying he had fallen. He had never had any fever or been sick. The lump in the region of the left thigh was now a little smaller. On examination there was definite limitation of abduction and rotation at the hip. Flexion was possible through 60°; there was a flexion deformity of 30°. The Mantoux test gave a positive reaction. An X ray picture, taken in the country, revealed shadows down the line of the femur which might suggest a diagnosis of old osteomyelitis, but examination of the acetabulum showed that the patient was suffering from tuberculous disease of the hip.

Cinema Films.

DR. G. W. MASON showed cinema films illustrating (*a*) right-sided spastic paralysis, and (*b*) artificial respiration in diaphragmatic paralysis.

Medical Societies.

THE MELBOURNE PÆDIATRIC SOCIETY.

A MEETING of the Melbourne Pædiatric Society was held at the Children's Hospital, Melbourne, on April 8, 1936, DR. C. H. OSBORN, the President, in the chair. The meeting took the form of a series of clinical demonstrations.

Pneumonia with Intracranial Complications.

DR. S. W. WILLIAMS showed for DR. STEWART FERGUSON a girl, thirteen years of age, who had been admitted to hospital on March 14, 1936, with vomiting, headache, drowsiness and upper abdominal pain of two days' duration. The presence of left basal pneumonia became apparent on the following day, and a day later it was noticed that the patient had a flaccid paralysis involving the left side of the palate and the left arm, including the shoulder girdle, with loss of sensation to pin-prick and cotton wool over the left forearm and the distal portion of the upper arm. The loss of sensation became complete and there was a distinct nasal intonation in the voice. On the next day a vague return of sensation to pin-prick was detected, and this improvement was progressive until very little sensory loss was observed. The febrile illness terminated by crisis and some improvement in the paralysis occurred, but there was still great weakness in the muscles and the palatal paralysis persisted. Within the period of ten days before the patient was admitted to hospital two younger members of the family were admitted with influenza. One of these children recovered quite quickly, but the other developed pneumonia and empyema and was still in hospital. A discussion was directed to the cause and nature of the intracranial complications.

DR. GRAEME ROBERTSON said that he had seen the girl on the day after the paralysis appeared. From the neurological point of view, apart from the fever and symptoms and signs attributable to the pneumonia, she had complained of severe frontal headache and displayed three groups of signs: (i) Complete left-sided palatal palsy and curtain-movement of the pharynx towards the right side; there was no loss of sensation over the fauces and pharynx, stimulation of either side producing brisk reflex movement to the right side. (ii) Complete flaccid paralysis of the left upper limb involving shoulder movements, with complete loss of all forms of sensation over the limb as far proximally as the junction of the middle and upper thirds of the arm. (iii) Kernig's sign was present on both sides and definite neck stiffness was elicited.

In considering the site and nature of the lesion in relation to these groups of signs, Dr. Robertson thought that the rapid development of the palatal and pharyngeal palsy, with complete escape of the sensory side, indicated a lesion of the motor nucleus of the glosso-pharyngeal nerve rather than a peripheral lesion, although some poisons causing a peripheral neuritis did affect chiefly the motor fibres. It was not beyond the realm of possibility that this was the route of delivery of the noxious agent to the central nervous system, but it was unilateral and the neurological manifestations occurred later than the visceral involvement. Dr. Robertson was influenced in deciding that a cortical lesion was present by the rapid development of motor, sensory and reflex loss in the arm, with rapid return of sensation to cotton wool and pin-point; slower return of discriminative sensibility; and toneless paralysis with partial improvement coincident with the sensory improvement, remaining stationary after a few days. He said that toxic polyneuritis was usually bilaterally symmetrical and that recovery was slow and progressive. The chief difficulty lay in the interpretation of the complete loss of the primary elements of sensation. Gross loss of sensation of pain was rare in cortical lesions; yet pain, with a definite march, did occur among the manifestations of sensory Jacksonian epilepsy. He had seen two thrombotic lesions of parietal branches of the middle cerebral artery accompanied by loss of sensibility to pain. Förster had described a case with injury to the upper portions of both parietal lobes showing loss of sensation to pin-prick up to a definite level. Stimulation of the post-central cortex did not cause elaborate appreciations, but more elemental dysæsthesiæ; it seemed likely that all sensory phenomena were appreciated and interpreted at the cortical level; a partial lesion interfered with the interpretation of combinations of primary sensations, the discriminative elements of sensation; a large lesion affecting all the incoming fibres from a particular region caused loss of all forms of sensation. Sensory

localization in the post-central region apparently corresponded roughly with motor localization in the pre-central region.

Dr. Robertson thought that the clinical course in the case under consideration fitted in well with a cortical localization. That the motor and sensory loss was confined to one arm excluded a lesion of the track below the cerebral level. At the last examination it was seen that the muscles of the arm were emerging from their initial flaccidity and that the left biceps jerk was more active than the right. There was some wasting of supraspinati and infraspinati, but very little of the remainder of the arm.

The third group of signs indicated meningeal involvement, more probably a response to the localized involvement than an actual meningitis. At all events, it favoured an inflammatory lesion rather than a vascular one.

Dr. Robertson's interpretation of the case was that there had been two lesions in the central nervous system, one in the right Betz cell area controlling the upper limb, with a surrounding area of temporary functional impairment, which subsided within a few days. There was a second lesion in the left side of the medulla. Without considering the implications of the pneumonia and the interesting family history, it was probable that the child had an encephalitis, possibly due to a virus.

Amyotonia Congenita.

DR. J. W. GRIEVE presented a male patient, aged four years and nine months, who was suffering from *amyotonia congenita* or Oppenheim's disease. The history was one of muscular weakness and hypotonicity dating from birth. The child was very late in sitting up and commenced crawling at the age of two years. His muscular power, however, had been gradually improving, and at the time of the meeting he was attempting to walk with support; his mental development had been quite normal. There were in the family three older children who were well and did not have any muscular weakness.

Examination revealed general hypotonicity and weakness of muscles without definite paralysis of any muscle groups. The limbs appeared relatively wasted, but Dr. Grieve thought that this might be attributed to disuse. The child had developed definite contractures at the wrists and ankles. The deformity of the wrist was one of flexion, with hyperextension at the metacarpo-phalangeal joints; the left foot was everted and the right inverted. Slight bilateral ptosis was observed and there was some weakness of the facial muscles. The isthmus of the thyreoid gland was visible and palpable. The child was very alert mentally.

Dr. Grieve discussed the diagnosis, which, on clinical grounds, he thought was one of *amyotonia congenita* or Oppenheim's disease. He contrasted this disease with progressive spinal muscular atrophy of the Werdnig-Hoffmann type. Pathologically the two diseases were similar in that there were atrophy and chromatolytic degeneration of the anterior horn cells; but the onset of the progressive spinal muscular atrophy usually occurred in the second half of the first year, and the disease tended to be steadily progressive, starting in the trunk, pelvic and shoulder girdles and extending peripherally; the intercostal muscles were also affected in the Werdnig-Hoffmann disease. Another interesting fact in this disease was that often more than one member of the family was affected. In *amyotonia congenita*, on the other hand, the disease was usually present from birth, no intercostal muscular weakness was present, and the condition often tended to improve steadily and complete recovery might result.

Dr. Grieve said that he showed the patient because of the rarity of the condition and to obtain an expression of opinion concerning the orthopædic management. In addition to the valgoid deformity of one foot and the varus position of the other, there was a tendency to wrist-drop and some ptosis with nystagmoid movement in the extreme lateral position of the eyeballs.

DR. GRAEME ROBERTSON agreed with Dr. Grieve's diagnosis and advised the use of light retentive apparatus to help the hypotonic muscles, and also frequent massage and movement. He thought that the ultimate prognosis was good, and recalled two patients of Dr. Collier who had become completely normal after about fifteen years.

Burns Treated with Mercurochrome.

DR. J. M. JENS, on behalf of DR. R. M. DOWNES, showed two children who had been under treatment for burns. A boy, J.B., four years of age, was admitted to hospital on March 22, 1936, on account of first and second degree burns covering the whole of the right buttock, the back of the right thigh and the upper half of the leg. Under general anæsthesia the affected area had been cleansed thoroughly before the first application of a 2% aqueous solution of mercurochrome. Without anæsthesia the mercurochrome dressings were repeated every hour for four hours, every two hours for a further twelve hours, and then every four hours until a good crust was obtained in forty-eight to sixty hours. As soon as it was seen that a thin layer of pus had formed beneath this crust, acriflavine emulsion (Australian Pharmaceutical Formulary) was applied in large amounts each day. With the exception of two small areas, a good clean surface was present by the tenth day and the patient was discharged on the twelfth day. Since then reinfection had occurred.

Dr. Jens also showed another patient who was still in the hospital and had been treated similarly for twelve days.

DR. C. H. OSBORN considered that it would be useful to analyse closely a series of patients' histories to obtain comparative figures of mortality and morbidity to see whether it could be shown conclusively that the method of treatment of burns which was at present in use at the hospital and which had been described by Dr. Jens, was superior to other methods. If it was proved to be superior, it should be adopted extensively.

DR. J. G. WHITAKER said that he did not think that Dr. Jens had placed sufficient emphasis on the details of the preliminary cleaning-up process under general anæsthesia.

Dr. Jens replied that ether, soap and benzine were used in this process, and, in reply to a question from Dr. A. P. Derham, Dr. Jens said that the subsequent applications were not particularly painful.

DR. G. B. MCCUMISKY said that, during his recent experience abroad, he had been very interested in the treatment of burns. He thought that the latest application was 20% tannic acid mixed with acriflavine (1 in 1,000 dilution); this application produced a thick scum with one spraying and its use was accompanied by very little shock. He had seen mercurochrome used as a 0·5% aqueous solution soaked on cloths and allowed to remain in contact with the wound for twelve hours. He had found that very often a transfusion of blood was given as a routine treatment to all patients under the age of four years who were suffering from serious burns. He too would like to see a comparison of results of the various modern methods.

DR. M. O. KENT HUGHES said that he would be interested to know whether anyone had formed an opinion of the comparative value of the cod liver oil emulsion with mercurochrome which was obtainable locally for use in the treatment of burns.

DR. C. H. OSBORN said that in a year as many as one hundred patients were admitted to the Children's Hospital with burns. Some time ago he had investigated three hundred and eighty of the histories when glycerine and picric acid was the standard application used. He had gained the impression that the mortality rate compared favourably with the present rate; not many patients died, other than those who died within the first twelve hours of admission; but the morbidity rates were higher; the patients were a long time in hospital, and many of them suffered considerably from sepsis. As the treatment in the early stages was conducted by the members of the

house staff, and such a large number of patients were involved, some organized system of comparison of methods was worthy of consideration.

DR. PAUL JONES considered that the patients shown by Dr. Jens illustrated very satisfactory results of the treatment he advocated. At the Royal Melbourne Hospital a mixture of 5% of tannic acid with acriflavine in a solution of one part in one thousand was being used, and on a recent occasion this application had been used on his own child with good results. He had tried mercurochrome privately, but had found it to be too expensive.

Chronic Pericarditis.

DR. A. W. RICHARDS, on behalf of DR. A. P. DERHAM, presented a girl, A.K., eight years of age, who had been admitted to the hospital originally on June 29, 1932, with the signs of generalized œdema and ascites. At that time it was found that the heart was enlarged, myocardial damage was present, and a loud systolic murmur, which might have been congenital, was audible; albuminuria was not present; there was no history of rheumatic infection. Under treatment with digitalis and other diuretics, and after six weeks of rest, the child was discharged from the ward. On seven occasions since then, however, she had been readmitted with signs of cardiac failure and had responded to treatment, though *paracentesis abdominis* was performed on the last occasion. She had been in the hospital since April 3, 1936, and appeared to be becoming progressively worse; the dyspnœa and the cyanosis were extreme, and generalized œdema could be felt up to the level of the lower ribs. The ascites was gross, and the circumference at the level of the umbilicus was 75 centimetres (thirty inches); there was great bulging of the precordium, and the apex beat was 12·5 centimetres (five inches) from the mid-line. For the first time, in addition to the systolic murmur, a diastolic murmur was audible, especially at the mitral area. The pulse rate ranged from 116 to 120 beats per minute, and the respiratory rate was forty. Crepitations could be heard at the bases of both lungs, but no fluid was present in the pleural cavities, nor was there any record of its occurrence at any time. The lower edge of the liver was hard and was about 10·0 centimetres (four inches) below the costal margin; the spleen was sufficiently enlarged to be palpable. Forty-eight ounces of ascitic fluid had been removed from the abdomen by paracentesis with great relief of the dyspnœa and cyanosis, but the symptoms and signs were recurring.

Dr. Derham said that the patient was shown with the object of stimulating a discussion on the differential diagnosis. He thought that the patient suffered from one of three conditions. The heart failure might be the result of a congenital abnormality of the heart or of rheumatic carditis, or the child might be the subject of polyserositis (Pick's disease). The illness had commenced when the child was only three years of age, and had been afebrile throughout; the Wassermann reaction had not been obtained when the child's blood was tested, and the blood sedimentation rate had been consistently recorded as a high horizontal line. Apparently a vicious circle was in operation and the diagnosis was not clear.

DR. IAN WOOD did not think that a congenital heart anomaly was present, and though the child was very young for rheumatic disease, the age was not an absolute bar to this diagnosis. Dr. John Poynton had described "the rheumatic condition" as one of widespread lesions, and it was necessary to recognize the rheumatic lung, rheumatic pleurisy and local rheumatic manifestations, such as perisplenitis, abdominal adhesions and inflammatory conditions of the liver and other organs. Dr. Wood thought that the child's condition would ultimately prove to be a widespread rheumatic infection, and the diastolic murmur seemed to him to confirm this view. The peritonitis might be of rheumatic origin and the result of portal obstruction.

DR. W. W. MCLAREN thought that the normal blood sedimentation rate was rather against the diagnosis of all the generalized infections, including rheumatic disease, and the duration of the signs of heart failure seemed to him to be excessively long for any infectious condition. Only recently in the wards two children had died of rheumatic heart disease within three weeks of admission; he thought that the course that the disease had run in the cases of these children was much more typical of rheumatic carditis.

DR. J. W. GRIEVE said that he had read somewhere that in the presence of heart failure the blood sedimentation rate was sometimes normal though an infection was present.

DR. IAN WOOD stated that in polycythæmia the blood sedimentation rate showed a slower drop, and that in anæmia the reverse happened; this child was probably polycythæmic; in this event the primary fall in the proteins of the blood would be the cause of the œdema of the heart failure.

Tuberculous Disease of the Hip with Hæmaturia.

DR. J. G. WHITAKER showed a boy, H.S., fifteen years of age, who had been treated for the past two years at the orthopædic branch of the hospital at Frankston on account of tuberculous disease of the right hip. The boy belonged to a family with a very bad history of tuberculosis, but the hip disease had responded favourably to treatment and a normal radiogram had been obtained. In the course of the preceding year, however, definite progressive destruction of the bone with subluxation of the hip had been observed; this was one of the cycles of events which were happening at Frankston, and the matter was the cause of much mental perturbation; the advisability of early arthrodesis was under consideration as a means of counteracting these complications. Fourteen months before the meeting the boy had had an attack of hæmaturia and left renal colic, which was repeated four days later; and within the past six months he had had a severe constitutional disturbance with pain and tenderness in the left loin. By cystoscopic examination the presence of hydronephrosis on the left side had been established. More recently a severe attack of left-sided renal pain had occurred and there was radiographic evidence of the presence of calculus in the left renal area with hydronephrosis. There was a large retention of "Uroselectan" on the left side, and in the pyelogram both pelves appeared large; colour had taken seven minutes to appear on the right side and twelve minutes on the left side. Dr. Whitaker said that he had considered either tuberculosis or calculus of the left kidney to be the cause of the hæmaturia. It was recognized that there was a fairly high incidence of renal tuberculosis among the subjects of bone tuberculosis, but he thought that it could be excluded in this case. With reference to renal calculus, which was so liable to occur in those patients who were subjected to long periods of recumbency, he wondered whether the condition was due to progressive decalcification and whether the decalcification was due to a superabundance of vitamin *D* and its influence on calcium metabolism. He recalled the death of a patient after laminectomy for tuberculous disease of the spine and the presence of a vesical calculus the size of a hen's egg. Dr. Whitaker had been diffident to operate on the kidney of the boy shown by him, although six months earlier the calculus had not been present; in the skiagram taken after the attack of hæmaturia in March, 1936, there was a shadow which suggested the presence of a large ureteral calculus. This suspicion was supported by a pyelogram done more recently, and Dr. Whitaker was of opinion that the boy had bilateral congenital hydronephrosis with ureteral calculus and multiple bilateral renal calculi. He wished to confine the discussion to the renal condition and said that he would be glad to know the views of those present on the prognosis and the underlying pathology. He wondered whether the boy was going to continue to manufacture calculi and whether he should operate on the ureteral calculus. Dr. Whitaker emphasized the importance of a fuller understanding of the process of

formation of calculi in tuberculous subjects because of the frequency of this complication at Frankston.

DR. PAUL JONES said that it was recognized elsewhere that renal calculi would form in people who were recumbent for a long time. He could not express an opinion on the ætiology, but wondered whether stagnation of urine, especially in the lower calyces, was a factor of importance. He would suggest that the patients should be given diuretics and postural treatment and a diet rich in fruit and vitamins.

DR. J. B. COLQUHOUN said that he was very interested in the question raised by Dr. Whitaker. Calculi were found more frequently in the subjects of so-called surgical tuberculosis than in sufferers from phthisis, and the explanation was on purely postural grounds; when the patients were treated in the sunshine, calcification became a very prominent feature. He had noticed that calcification occurred in the walls of abscesses in the patients at Frankston, but that there was an absence of this phenomenon at the Austin Hospital at Heidelberg, where there was not nearly so much exposure to sunshine. Another factor was the size of the patient; a big and heavy patient, such as the lad shown by Dr. Whitaker, when placed in a large plaster or on a splint, would be liable to lie for a long time unless special care was taken to turn him frequently. Dr. Colquhoun had often wondered whether calculi could be dissolved by any form of medicinal treatment, but he did not know of anything that was satisfactory. He thought that the ureteral stone should be removed from Dr. Whitaker's patient; he did not think it likely that further calculi would be formed.

Non-Specific Arthritis of the Ankle.

DR. C. H. OSBORN showed a boy, T.H., eight years of age, who came under his notice first in November, 1934, because the right ankle had been swollen for four months. It was thought that the swelling had resulted from kicking a football, but the injury, if any, was very mild. He had for two months been receiving treatment once a week from a professional masseur, but the ankle was steadily getting worse. He had a little pain and a slight rise of temperature, and some fluid was definitely present in the joint. At that time and ever since radiographic investigation had revealed no abnormality; the Mantoux test had been applied repeatedly with negative results. The movements at the ankle were painless and practically unlimited; on one occasion only had it been noticed that there was some slight limitation of inversion. The ankle joint was hot and full of fluid, and the patient limped. Dr. Osborn said that he had immobilized the leg in plaster for a week, and two months later had applied a plaster fitted with a walking iron. He had manipulated the joint under general anæsthesia; the movement was free and no cracking of adhesions had occurred, but there had been no improvement in the condition. Afterwards a series of blood sedimentation rate investigations had shown positive improvement in the curves. In August, 1935, the boy's tonsils were removed and the ankle joint had gradually improved and he had been bearing weight on the leg for some time. The blood had been tested for syphilis on several occasions with negative findings.

Dr. Osborn said that he and Dr. Price had been very interested in the condition which they had come to call non-specific arthritis in joints. The patients whom they had seen had all had hydrops of the ankle or hip joint; the joint had been swollen and red, but not very painful. They regarded the condition as being due to coccal infection, and the principal interest was to be able to establish the diagnosis in the early stages.

DR. ERIC PRICE said that it was difficult to decide in the case of the boy shown by Dr. Osborn whether the condition was toxic or due to coccal infection. He recalled a similar case from which a coccus had been recovered, which might have been a pneumococcus. He drew attention to the fact that in certain cases tuberculous bone lesions were regarded as being primarily synovial, with the subsequent development of the bony focus. He regarded the Mantoux test as being very useful in the early stage of the disease. If the result of the test was negative, he regarded the condition as non-specific. Dr. Price wondered whether spastic flat-foot could be classed in the same category.

DR. J. G. WHITAKER said that he thought that the condition present was similar to the one which had been called intermittent hydrarthrosis and which was sometimes bilateral. There was a tendency for the fluid to disappear as the patient got older, without any damage to the joint; the fluid was a simple albuminous secretion, and there was a definite tendency for recovery to take place.

DR. M. O. KENT HUGHES referred to some examples seen in the last eighteen months, in which effusions in the knee joint were due to the formation of adhesions after knocks; he thought that this was a possible explanation of the case shown by Dr. Osborn.

DR. J. W. GRIEVE, speaking as a physician, said that it was a fairly common experience to encounter patients with quiet effusions in hip or ankle joints; quite a number of them cleared up in a few weeks on immobilization or after treatment by extension. He had been struck by the fact that there was as a rule some association with follicular tonsillitis.

DR. MURRAY TALLENT said that he remembered a patient at the Royal Melbourne Hospital with spastic flat-foot who developed multiple swollen joints.

DR. J. B. COLQUHOUN mentioned the history of a patient at the hospital in whose case Dr. Reginald Webster had identified *Bacillus tuberculosis* from the fluid removed by aspiration. There had been no skiagraphic evidence of involvement of the bone, and the patient had become perfectly well after five years. Dr. Colquhoun said that if the Mantoux test gave no reaction there was a tendency to forget the focalization test. It was difficult to keep the organisms alive in joint fluid or to culture them.

In reply, Dr. Osborn referred to Dr. Grieve's statement that such patients were frequently encountered; this was not Dr. Osborn's experience of this long-standing arthritis with very little rise in temperature. Examples of ordinary synovitis recurring after injury were in a totally different category. The term intermittent hydrarthrosis used by Dr. Whitaker did not appear to him as suitable, and when tuberculosis, syphilis and gonorrhœa could be excluded as ætiological factors he thought the term non-specific arthritis was more satisfactory, though he admitted that the onus of proof lay on the person who excluded tuberculosis.

Acute Arthritis of the Hip Joint.

Dr. Osborn also showed a boy, S.H., who had been operated on by Dr. Upjohn at the end of November, 1935, for acute arthritis of the left hip joint. At that time the boy was very ill; a lot of pus was evacuated from the joint and a rupture had been present deep to the iliacus muscle. The patient made a good recovery and was treated by weight extension of both legs in bed. The skiagram on December 14, 1935, showed sequestration of the capital epiphysis of the femur and a skiagram taken on January 16, 1936, showed that absorption of the epiphysis was in progress. When Dr. Osborn took charge of the boy in January, the wounds had almost stopped discharging and a fixed flexion deformity of 45° was present with some adduction deformity; the pelvis was tilted and a great degree of lordosis was present. Dr. Osborn had shown the patient to illustrate the use of the plaster popularized by Dame Agnes Hunt for the correction of lordosis. On February 26, 1936, he had put the right leg up in full flexion with slight abduction of the hip joint and flexion of the knee joint to a right angle; extension was applied to the left leg on a Thomas's splint with hyperextension on a Bradford frame. The lordosis was corrected and Dr. Osborn said that he was surprised at the degree of movement at the affected hip joint. The other point of interest discussed by Dr. Osborn had

reference to the relative merits of different methods of approach to the hip joint at operation. He had been of the opinion that the posterior approach was the best, but ankylosis would occur and he put the patients in plaster to avoid dislocation with abduction. With the anterior approach, as in the present case, a movable joint had been obtained and treatment by Hamilton Russell extension had been very successful. He thought that in acute cases the present method should be adopted, but that when the patient was operated on at a later stage the posterior approach was to be preferred. In either case the patient should be put on a Bradford frame, and the secret of the prevention of pressure sores was to prolong the plaster up to or higher than the mid-dorsal position.

Dr. Price said that he thought that the method of treatment employed by Dr. Osborn was excellent, and he only wished to discuss the method of attack. He thought that the anterior approach should be avoided because of the difficulty in drainage, the simplicity of the muscle-splitting posterior approach, and the good results obtained by it. In some cases a lateral approach might be considered.

Pathological Specimens.

DR. REGINALD WEBSTER showed under the microscope a Fontana preparation of *Treponema pallidum* obtained from a primary genital sore in a girl ten years of age. Within the subsequent two weeks a roseolar rash had developed and the girl's serum had yielded the Wassermann reaction.

Dr. Webster also demonstrated a number of very interesting pathological preparations, which included one of complete transposition of viscera. The right lung had two lobes and the left lung three lobes; dextrocardia was present and the liver was in the left hypochondrium, with the spleen on the right side; the caecum and the appendix were in the left iliac fossa and the sigmoid colon was in the right side of the pelvis.

Other specimens illustrated the lesions of fulminant bacillary dysentery in an infant with recovery of the *Bacillus dysentericus* (Flexner); multiple pulmonary metastases from a child who died six months after nephrectomy undertaken for a Wilms's embryoma of the kidney; bowel which failed to recover after reduction of an ileo-colic intussusception; specimens of agonal intussusceptions and of horseshoe kidney; a specimen showing the condition of the pylorus six months after the Rammstedt operation for congenital pyloric stenosis, and a specimen in which the first part of the duodenum terminated blindly.

Post-Graduate Work.

LECTURE AND DEMONSTRATIONS ON UTERINE PROLAPSE.

THE New South Wales Post-Graduate Committee in Medicine announces the following programme of lecture and demonstrations by Dr. T. G. Stevens, Consulting Surgeon, Saint Mary's Hospital, the Hospital for Women, Soho Square, and the Queen Charlotte's Lying-in Hospital, London.

Tuesday, May 19.

2.30 p.m.—Operative demonstration at Lewisham Hospital.

Thursday, May 21.

2.30 p.m.—Operative demonstration at the Royal North Shore Hospital.

(Each operative demonstration is limited to twelve and the fee is 10s. 6d.; tickets may be obtained on application to the Secretary, the New South Wales Post-Graduate Committee in Medicine, the University of Sydney.)

Tuesday, May 26.

8.30 p.m.—Lecture, at the Robert H. Todd Assembly Hall, 135, Macquarie Street, Sydney: "Prolapse: Its Management and Treatment".

The fee for admission will be five shillings. Admission will be by ticket only. Tickets may be obtained at the door or by application to the Secretary, the New South Wales Post-Graduate Committee in Medicine, the University of Sydney, Sydney.

Correspondence.

CONE SHELL MOLLUSC POISONING.

SIR: I was interested in the cases of cone shell poisoning recently recorded in this journal. About ten years ago I was marooned for six weeks on Matty Island, a coral atoll north of New Guinea, owing to an oversight on the part of the ship's captain. It is out of sight of all land, and during my enforced stay there I was quite out of touch with the outside world, with not even a glimpse of ship or sail. The island is inhabited by a straight-haired, dark-skinned people, a mixture of Melanesian and Malay, according to Professor Macmillan Brown, to whom I gave a list of many of their words, and is surrounded by a large expanse of flat reef, on the outside edge of which in heavy north-westerly weather the surf breaks with a noise like thunder, night and day, the spray flying up to a height of forty feet, while the tall coconut palms, as seen from the reef, writhe, twist and sway in all directions, as though in the utmost agony, in a most grotesque way, and one marvels that they are able to stand up to the strain. Among the many weird things from the reef that the natives brought me for food were numerous kinds of the *Conus* shell, edible seaweed, and crabs, including the large coconut crab, which is more like a lobster in shape. I found the *Conus* mollusc such good eating that I used to collect them myself on the reef and was quite unaware of the danger from them, though I used to be interested in watching them throwing out the arm with the attached sting as the drying began to affect them; but by this time, luckily for me, they had been transferred to a plaited coconut basket. In eating them, they are withdrawn from the shell by pulling on the arm, which is lifted from the slot in the shell like the blade of a clasp knife from its groove. Dr. Flecker says that the *Conus geographus* is easily distinguished by its gay colouring, but almost all the varieties found here might be called gaily coloured, being streaked and striped with various shades of brownish red and purplish red.

Though no doubt a matter of small moment, would it not be more in accordance with our wording to speak of being "stung" by them, rather than "bitten"?

Yours, etc.,

ERIC POCKLEY.

Killara,
New South Wales,
April 20, 1936.

PSYCHOANALYSIS.

SIR: In a letter in your journal dated April 5, 1936, Dr. McGeorge directs my attention to an error when I state that Freud's work was commenced forty years ago. I regret that I used the word "forty" more in a general than in a mathematical sense.

Freud's first publication was in conjunction with Breuer in the *Neurologisches Zentralblatt*, 1893, and the first essay by Freud alone was in the *Archives de Neurologie*, 1893.

These essays, with others dating from 1894-1905, are published in the *Sammlung Kleiner Schriften zur Neurosenlehre*, 1909.

The correct statement should have been that Freud's work commenced in 1893—forty-three years ago.

Yours, etc.,

JOHN K. ADEY.

Receiving House,
Melbourne,
April 21, 1936.

TUBERCULOUS MENINGITIS WITH RECOVERY.

SIR: I was interested to read Dr. Bertrand Cook's letter in this week's issue of your journal.

The prognosis of tuberculous meningitis is such a hopeless one that I prefer not to make an irretrievable diagnosis, unless it can be substantiated by the demonstration of tubercle bacilli in the cerebro-spinal fluid.

Tubercle bacilli can be found in the cerebro-spinal fluid in the great majority of cases, provided the pathologist is prepared to devote the time necessary for the search and is supplied with a sufficient quantity of fluid. Tubercle bacilli were found in 135 of 137 cases observed by Hemenway and in 100 of 102 cases observed by Bernstein ("Osler's Modern Medicine"). I am not convinced that a family history of phthisis, positive cutaneous tests or an X ray picture of an alleged primary focus in the lung can be accepted as proving a tuberculous ætiology in the case of meningitis which Dr. Bertrand Cook has reported. In fact, the diagnosis cannot be proved either way and is a matter of opinion. Perhaps in that respect we can agree to differ.

Yours, etc.,

JOHN A. McLEAN.

12, Collins Street,
Melbourne,
April 22, 1936.

HYOSCINE IN PARALYSIS AGITANS.

SIR: *Re* hyoscine in *paralysis agitans*. I read with interest in THE MEDICAL JOURNAL OF AUSTRALIA of February 22, 1936, a "Current Comment" entitled "Stramonium in Parkinsonism", in which reference is made to a paper by H. Stott. Therein he points out that hyoscine reduces the tremor but has no effect on the rigidity of *paralysis agitans*.

I have had under my care for some weeks past an elderly female patient afflicted with this disease in a fairly advanced state. She has been treated with hyoscine administered orally in gradually increasing doses until she is now receiving one-hundredth of a grain thrice daily. Not only has the tremor been markedly reduced, but the rigidity has been considerably diminished, and this fact is borne out both by the patient herself and by a member of her family who is in constant attendance upon her. If the drug be intermitted for one or two days, both tremor and rigidity recur to a degree which is quite obvious.

The patient is in better general health than she has been for some time past, and so far no toxic symptoms have developed.

I can, however, recall having seen other cases treated with this drug in which no appreciable diminution of rigidity resulted.

I have not yet tried the effect of stramonium on this patient.

Yours, etc.,

R. H. BRENT, M.B., B.S.

Taroom,
Queensland,
April 27, 1936.

Proceedings of the Australian Medical Boards.

QUEENSLAND.

THE undermentioned have been registered, pursuant to the provisions of *The Medical Acts*, 1925 *to* 1935, of Queensland, as duly qualified medical practitioners:

O'Connor, John Mackey, M.B., B.S., 1929 (Univ. Melbourne), Brisbane.

O'Neill, Niall Eugene, M.B., B.S., 1936 (Univ. Sydney), Brisbane.

Skyring, Doris Una, M.B., B.S., 1935 (Univ. Sydney), Rockhampton.

Statham, Clive Laurence, M.B., 1936 (Univ. Sydney), Brisbane.

Winton, Ronald Richmond, M.B., B.S., 1936 (Univ. Sydney), Brisbane.

Wright, Alison McQueen, M.B., B.S., 1935 (Univ. Melbourne), Brisbane.

Gorman, John Lawrence, M.B., B.S., 1936 (Univ. Melbourne), Brisbane.

May, Garth Mervyn Sydney, M.B., B.S., 1936 (Univ. Melbourne), Brisbane.

Punch, Francis Michael Greenway, M.B., Ch.M., 1926 (Univ. Sydney), Brisbane.

Watson, Alexander Thurston, M.B., B.S., 1933 (Univ. Sydney), Collinsville.

Wilson, Joseph Besnard, M.B., B.S., 1921 (Univ. Sydney), Mount Isa.

NOTICE.

WE have been asked to insert the following notice.

THE ROYAL SOCIETY.

E. Alan Johnston and Lawrence Research Fellowship.

Applications are invited by the Council of the Royal Society for the E. Alan Johnston and Lawrence Research Fellowship in Medicine, tenable in any hospital or medical school in the British Isles. Candidates should supply the usual personal details and give the names of two referees. Testimonials will not be considered. Applicants and referees at a distance may write direct to the address given below without first obtaining forms. The subject of the proposed research, and the place at which it would be carried out, together with the name of the head of the department, should be given.

The appointment will be for two years in the first instance, from October 1, 1936, and will be renewable annually up to a total of five years. It will be subject to the conditions governing Royal Society research appointments. The stipend will be £700 per annum, with superannuation benefits.

Applications should be made on forms to be obtained from the Assistant Secretary, The Royal Society, Burlington House, London, W.1, and should be received as early as possible, in any case not later than Saturday, June 6.

Corrigendum.

AN error has occurred in the report of The Australian Conference on Crippled Children, published in the issue of May 2, 1936. At page 626 Dr. Douglas Galbraith is reported to have said that the cost per bed at the orthopædic section of the Children's Hospital at Frankston, Victoria, was £3 10s. per week. The figure mentioned was actually £2 10s.

Books Received.

A GLASGOW MANUAL OF OBSTETRICS, by Samuel J. Cameron, M.B., F.R.F.P.S., F.C.O.G., John Hewitt, M.B., Ch.B., F.C.O.G., Robert A. Lennie, M.D., F.R.F.P.S., F.C.O.G., Ellen D. Morton, M.B., Ch.B., M.C.O.G.; Second Edition; 1936. London: Edward Arnold and Company. Medium 8vo, pp. 619, with illustrations. Price: 21s. net.

Diary for the Month.

MAY 12.—Tasmanian Branch, B.M.A.: Branch.
MAY 12.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
MAY 19.—Tasmanian Branch, B.M.A.: Council.
MAY 19.—New South Wales Branch, B.M.A.: Ethics Committee.
MAY 20.—Western Australian Branch, B.M.A.: Branch.
MAY 22.—Queensland Branch, B.M.A.: Council.
MAY 26.—New South Wales Branch, B.M.A.: Medical Politics Committee.
MAY 27.—Victorian Branch, B.M.A.: Council.
MAY 28.—South Australian Branch, B.M.A.: Branch.
MAY 28.—New South Wales Branch, B.M.A.: Branch.
JUNE 1.—New South Wales Branch, B.M.A.: Organization and Science Committee.
JUNE 2.—Tasmanian Branch, B.M.A.: Council.
JUNE 3.—Western Australian Branch, B.M.A.: Council.
JUNE 3.—Victorian Branch, B.M.A.: Branch.
JUNE 4.—New South Wales Branch, B.M.A.: Clinical Meeting.
JUNE 4.—South Australian Branch, B.M.A.: Council.
JUNE 5.—Queensland Branch, B.M.A.: Branch.
JUNE 9.—Tasmanian Branch, B.M.A.: Branch.
JUNE 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

Medical Appointments.

Dr. L. G. Tassie, pursuant to the provisions of the *Workmen's Compensation Act*, 1932, has been appointed a Member of the Medical Board of Port Pirie, South Australia.

* * *

Dr. R. G. Burnard has been appointed Honorary Commissioner in South Australia to inquire into and report upon matters relating to contract medical practice and national insurance in Great Britain.

* * *

Dr. D. M. McWhae and Dr. M. K. Moss, in pursuance of Section 94 of *The Lunacy Act*, 1903-20, have been appointed Visitors to the Claremont, Greenplace and Whitby Falls Mental Hospitals, Western Australia.

* * *

Dr. I. H. Cowling, pursuant to the provisions of the *Workers' Compensation Acts*, has been appointed Certifying Medical Practitioner at Alexandra, Victoria.

* * *

Dr. J. P. Barry has been appointed Government Medical Officer at Woodburn, New South Wales.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser", pages xvi-xviii.

CHILDREN'S HOSPITAL, CARLTON, VICTORIA: Honorary Attending Surgeon.

ROYAL ALEXANDRA HOSPITAL FOR CHILDREN, SYDNEY, NEW SOUTH WALES: Honorary Officers.

ROYAL HOSPITAL FOR WOMEN, PADDINGTON, NEW SOUTH WALES: Resident Medical Officers.

SYDNEY HOSPITAL, SYDNEY, NEW SOUTH WALES: Honorary Gynæcological Surgeon.

THE NEW SOUTH WALES MASONIC HOSPITAL, SYDNEY, NEW SOUTH WALES: Resident Medical Officer.

THE PUBLIC SERVICE BOARD, SYDNEY, NEW SOUTH WALES: Medical Officer.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCHES.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 135, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Brisbane Associate Friendly Societies' Medical Institute. Chillagoe Hospital. Richmond District Hospital, North Queensland. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY Hospital are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.
SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide.	All Lodge appointments in South Australia. All Contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 205, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (Wellington Division): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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